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FILE 'CAPLUS' ENTERED AT 15:55:04 ON 23 SEP 2004

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FILE COVERS 1907 - 23 Sep 2004 VOL 141 ISS 13

FILE LAST UPDATED: 22 Sep 2004 (20040922/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

*inventor
search*

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:64013 CAPLUS

DOCUMENT NUMBER: 134:110477

ENTRY DATE: Entered STN: 26 Jan 2001

TITLE: **Cyclic peptidomimetic** urokinase

INVENTOR(S): receptor antagonists and therapeutic use thereof

Wilhelm, Olaf; **Kessler, Horst; Burgle, Markus**; Potthoff, Nils; Schmiedeberg, Niko

PATENT ASSIGNEE(S): Wilex Biotechnology G.m.b.H., Germany

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

INT. PATENT CLASSIF.:

MAIN:

C07K007-00

CLASSIFICATION: 1-12 (Pharmacology)

Section cross-reference(s): 63

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|------------------|----------|
| WO 2001005811 | A2 | 20010125 | WO 2000-EP6905 | 20000719 |
| WO 2001005811 | A3 | 20010719 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| DE 19933701 | A1 | 20010125 | DE 1999-19933701 | 19990719 |
| EP 1194531 | A2 | 20020410 | EP 2000-951406 | 20000719 |

EP 1194531 B1 20040512
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 AT 266722 E 20040515 AT 2000-951406 20000719
 PRIORITY APPLN. INFO.: DE 1999-19933701 A 19990719
 WO 2000-EP6905 W 20000719

PATENT CLASSIFICATION CODES:

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------------------------------|-------|------------------------------------|
| WO 2001005811 | ICM | C07K007-00 |
| OTHER SOURCE(S): MARPAT 134:110477 | | |

ABSTRACT:

Cyclic peptide compds. are provided which are used as inhibitors of urokinase binding to urokinase receptors. The cyclic peptide compds. are suitable for use as pharmaceutical active ingredients to combat diseases which are mediated by urokinase and urokinase receptor.

SUPPL. TERM: peptide cyclic urokinase receptor binding inhibition
 therapeutic; cyclic peptidomimetic urokinase receptor
 binding inhibition therapeutic

INDEX TERM: Stability
 (against protease; cyclic peptidomimetic urokinase
 receptor antagonists and therapeutic use)

INDEX TERM: Angiogenesis inhibitors
 Antitumor agents
 Drug delivery systems
 Drug targeting
 Peptidomimetics
 (cyclic peptidomimetic urokinase receptor antagonists and
 therapeutic use)

INDEX TERM: Urokinase-type plasminogen activator receptors
 ROLE: BPR (Biological process); BSU (Biological study,
 unclassified); BIOL (Biological study); PROC (Process)
 (cyclic peptidomimetic urokinase receptor antagonists and
 therapeutic use)

INDEX TERM: Peptides, biological studies
 ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); THU (Therapeutic use);
 BIOL (Biological study); USES (Uses)
 (cyclic; cyclic peptidomimetic urokinase receptor
 antagonists and therapeutic use)

INDEX TERM: Blood serum
 (stability in; cyclic peptidomimetic urokinase receptor
 antagonists and therapeutic use)

INDEX TERM: 321147-43-7P 321147-49-3P 321147-63-1P 321147-67-5P
 321147-85-7P 321147-91-5P 321147-95-9P
 ROLE: BAC (Biological activity or effector, except adverse);
 BPR (Biological process); BSU (Biological study,
 unclassified); PRP (Properties); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); PROC (Process); USES (Uses)
 (cyclic peptidomimetic urokinase receptor antagonists and
 therapeutic use)

INDEX TERM: 9001-90-5, Plasmin
 ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); BIOL (Biological
 study)
 (cyclic peptidomimetic urokinase receptor antagonists and
 therapeutic use)

INDEX TERM: 214895-18-8P 321147-47-1P 321147-51-7P 321147-53-9P
 321147-55-1P 321147-57-3P 321147-59-5P 321147-61-9P
 321147-65-3P 321147-69-7P 321147-71-1P 321147-73-3P

321147-75-5P 321147-77-7P 321147-79-9P 321147-81-3P
321147-83-5P 321147-87-9P 321147-89-1P 321147-93-7P
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); PRP (Properties); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
(cyclic peptidomimetic urokinase receptor antagonists and
therapeutic use)

INDEX TERM:

321147-43-7D, amino acid-substitution derivs.
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic peptidomimetic urokinase receptor antagonists and
therapeutic use)

INDEX TERM:

9039-53-6, Urokinase plasminogen activator
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(cyclic peptidomimetic urokinase receptor antagonists and
therapeutic use)

INDEX TERM:

9001-92-7, Protease
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); BIOL (Biological
study)
(stability against; cyclic peptidomimetic urokinase
receptor antagonists and therapeutic use)

=> fil reg; d sqide l14 1-19

FILE 'REGISTRY' ENTERED AT 16:09:50 ON 23 SEP 2004

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L7 (19)SEA FILE=REGISTRY ABB=ON [CDE'DAB''PEN''DPR''ORN'K] [DEN] ['DAB'
'DPR'H'CIT''NLE'K] [Y'THI'W'PHG'A] [FW'THI''PHG'] [SV] [DEN] [IVA'AB
U''AIB'] [CDE'DPR''DAB''PEN''ORN'K]W/SQSP
L14 19 SEA FILE=REGISTRY ABB=ON L7 AND (BRIDG? OR CYCLIC)/NTE

L14 ANSWER 1 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 390391-14-7 REGISTRY 6

CN L-Cysteine, L-cysteinyl-L-valyl-L-cysteinyl-L-asparaginyl-L-lysyl-L-alanyl-
L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-L-tryptophyl-
, cyclic (1.fwdarw.13)-disulfide (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 13

NTE

| type | location | description |
|--------|----------------|------------------|
| bridge | Cys-1 - Cys-13 | disulfide bridge |

SEQ 1 CVCNKAFSNI CWC

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HITS AT: 3-12

MF C63 H93 N17 O17 S4

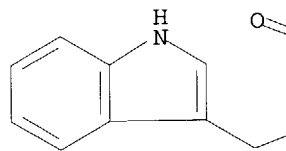
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

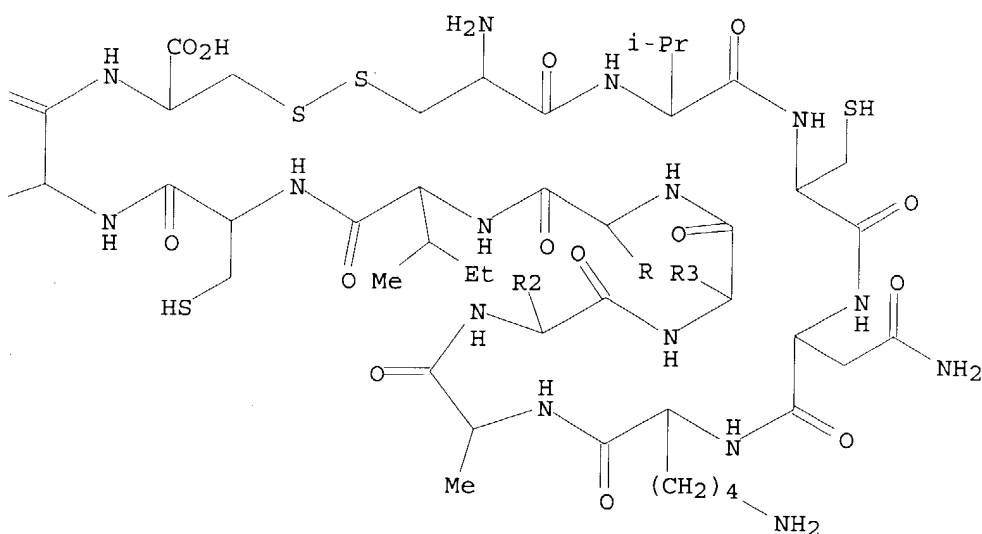
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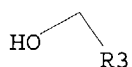
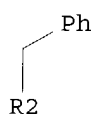
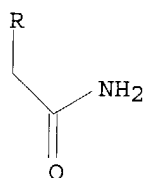
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doesn't have
"approved" shortcut
symbols for all of
the uncommon AA's
listed by inventors
Not searchable in
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homocitrulline
homophenylalanine
tetrahydroisoguanine-3-
carboxylic acid

1-naphthylalanine
2-naphthylalanine
tert-leucine

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PAGE 2-A



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 2 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-93-7 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-3-(1-naphthalenyl)-L-alanyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 28: PN: W00105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified (modifications unspecified)

| type | location | description |
|------|----------|-------------|
|------|----------|-------------|

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 3 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 321147-91-5 REGISTRY
 CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-norleucyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 27: PN: WO0105811 PAGE: 17-29 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE

| type | location | description |
|----------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| uncommon | Nle-3 - | - |

PATENT ANNOTATIONS (PNTE):

| Sequence | Patent |
|-----------|---------------------------------------|
| Source | Reference |
| Not Given | WO2001005811 claimed PAGE 17-29 |

SEQ 1 CNXYFSNICW

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HITS AT: 1-10

MF C58 H77 N13 O15 S2

SR CA

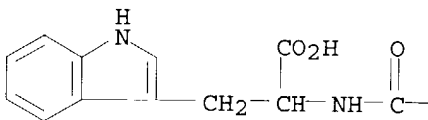
LC STN Files: CA, CAPLUS, CASREACT, PROUSDDR, TOXCENTER

DT.CA Caplus document type: Journal; Patent

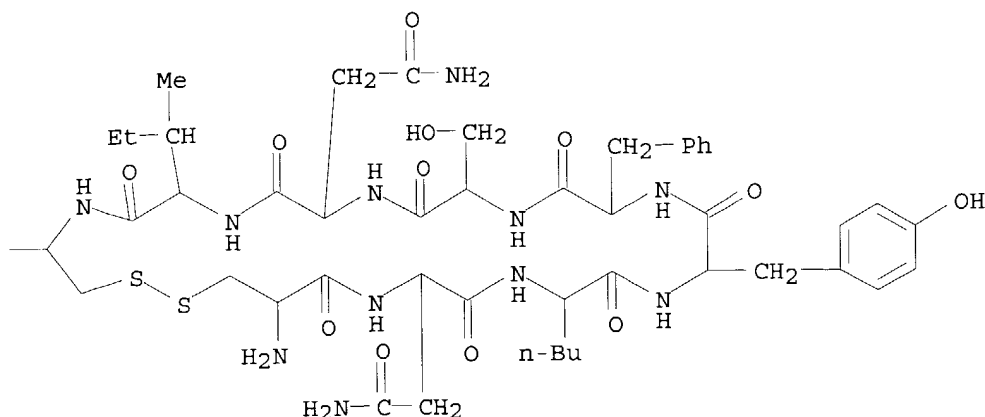
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

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3 REFERENCES IN FILE CA (1907 TO DATE)
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 4 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 321147-87-9 REGISTRY
 CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-3-(2-naphthalenyl)-L-alanyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 25: PN: WO0105811 PAGE: 17-29 claimed protein
 CN 5: PN: DE10209030 PAGE: 9 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified (modifications unspecified)

| type | location | description |
|--------------|---------------|------------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| modification | Ala-4 | 2-naphthalenyl<2-Naph> |

PATENT ANNOTATIONS (PNTE):

Sequence | Patent
 Source | Reference
 =====+=====

| | |
|-----------|--------------|
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKAFSNICW

HITS AT: 1-10

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C62 H80 N14 O14 S2

SR CA

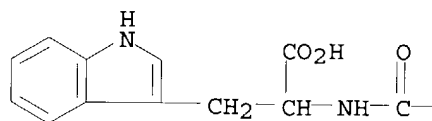
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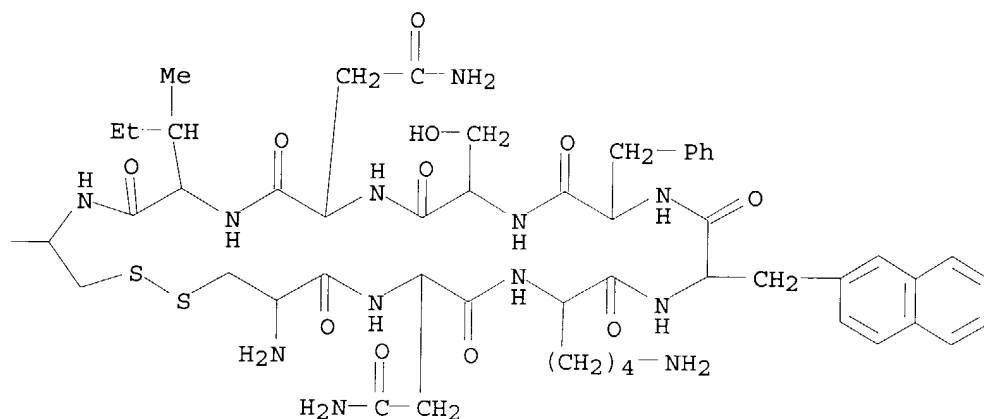
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RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

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3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 5 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-83-5 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-3-cyclohexyl-L-alanyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 23: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified (modifications unspecified)

| type | ----- | location | ----- | description |
|--------------|-------|----------|-------|------------------|
| bridge | Cys-1 | - | Cys-9 | disulfide bridge |
| modification | Ala-4 | - | - | cyclohexyl<Chx> |

PATENT ANNOTATIONS (PNTE):

Sequence | Patent

Source | Reference

=====+=====

Not Given | WO2001005811

| claimed PAGE

|17-29

SEQ 1 CNKAFSNIW

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HITS AT: 1-10

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MF C58 H84 N14 O14 S2

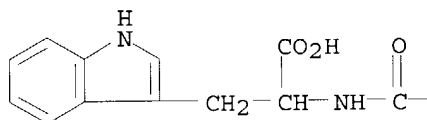
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LC STN Files: CA, CAPLUS, TOXCENTER

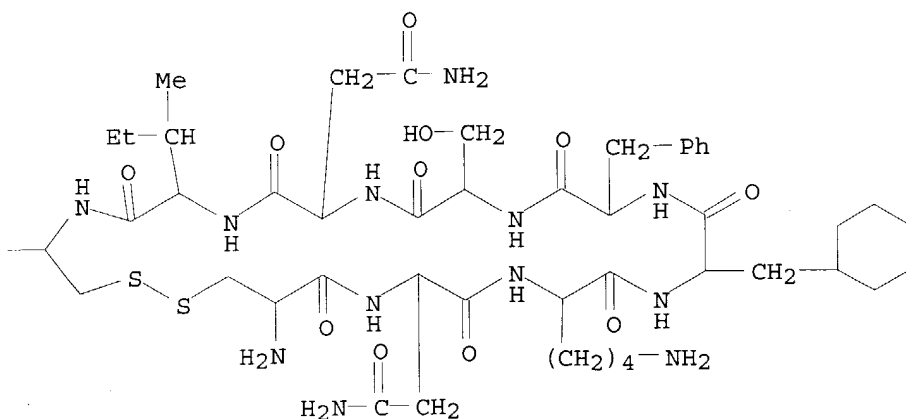
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

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PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 6 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-81-3 REGISTRY

CN L-Tryptophan, 3-mercapto-D-valyl-L-asparaginyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-3-mercapto-L-valyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: W00105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE

| type | location | | description |
|----------|----------|---------|------------------|
| bridge | Pen-1 | - Pen-9 | disulfide bridge |
| uncommon | Pen-1 | - | - |
| uncommon | Pen-9 | - | - |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| ===== | ===== |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 XNKYFSNIXW

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HITS AT: 1-10

MF C62 H86 N14 O15 S2

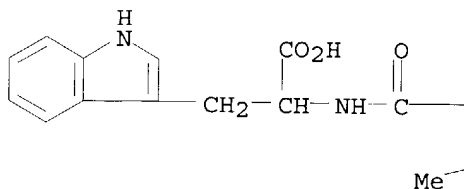
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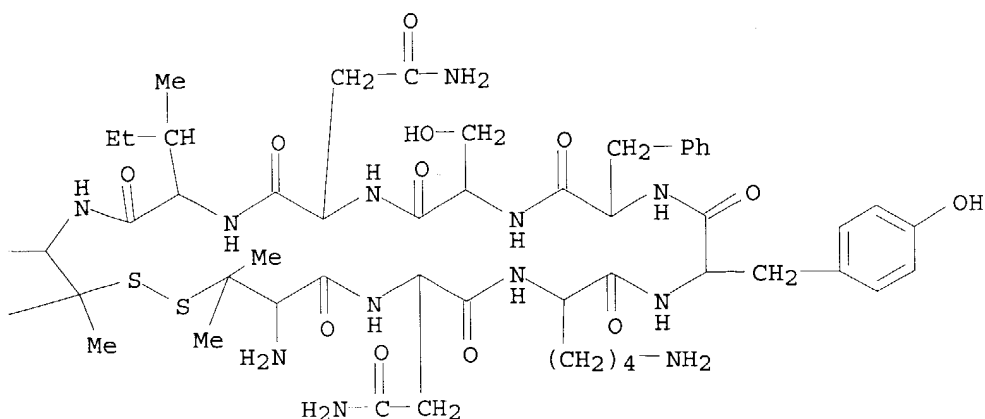
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

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PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 7 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 321147-79-9 REGISTRY
 CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-3-cyclohexyl-L-alanyl-L-cysteinyl-, cyclic
 (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 21: PN: WO0105811 PAGE: 17-29 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE modified (modifications unspecified)

| type | location | description |
|--------------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| modification | Ala-8 | cyclohexyl<Chx> |

PATENT ANNOTATIONS (PNTE):

| Sequence | Patent |
|-----------|--------------|
| Source | Reference |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKYFSNACW

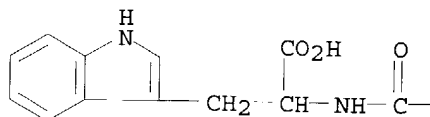
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LC STN Files: CA, CAPLUS, TOXCENTER

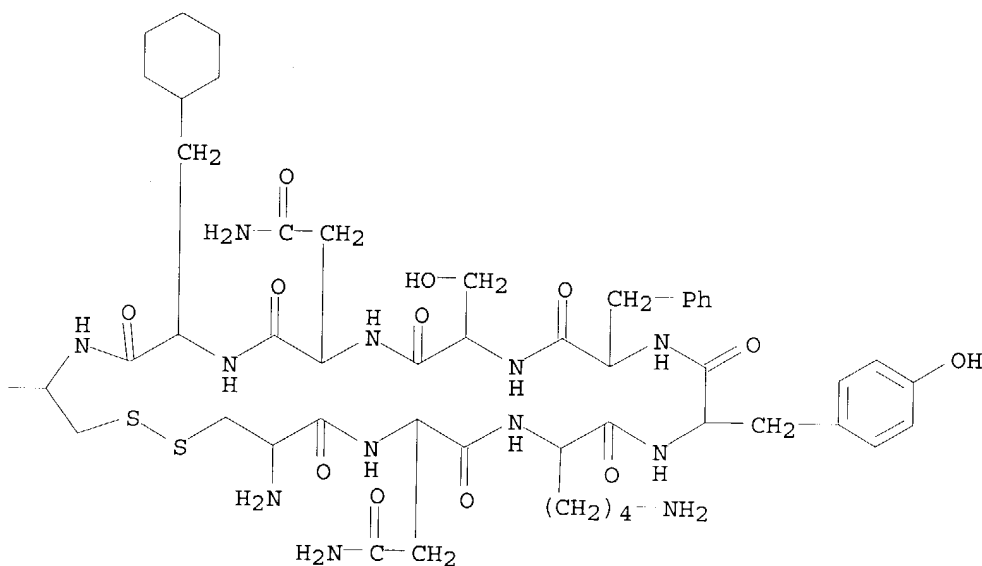
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 8 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-77-7 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-N6-(aminocarbonyl)-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 20: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified (modifications unspecified)

| type | location | description |
|------|----------|-------------|
|------|----------|-------------|

bridge Cys-1 - Cys-9 disulfide bridge
modification Lys-3 - aminocarbonyl<Cbm>

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| ===== | ===== |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKYFSNICW

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RELATED SEQUENCES AVAILABLE WITH SEQLINK

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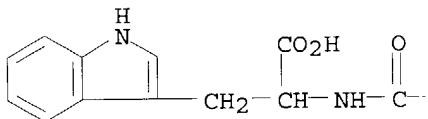
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LC STN Files: CA, CAPLUS, TOXCENTER

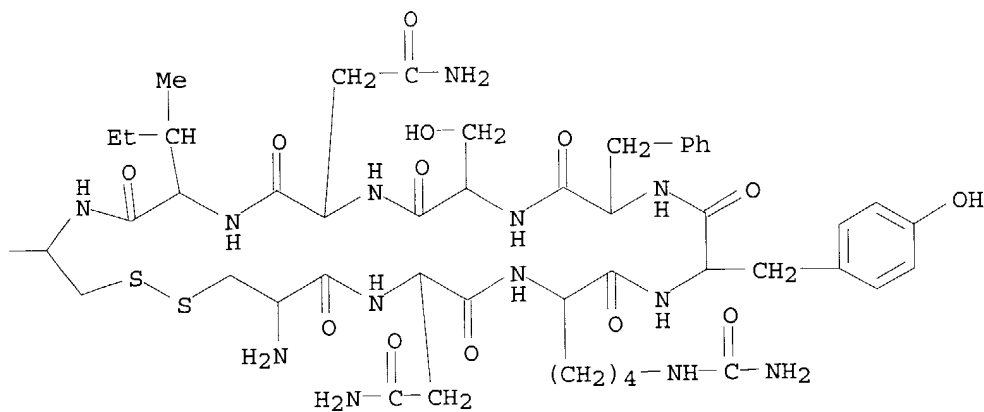
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RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 9 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 321147-75-5 REGISTRY
CN L-Tryptophan, D-cysteiny-L-asparaginy-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginy-L-isoleucyl-3-mercapto-L-valyl-, cyclic
(1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 19: PN: WO0105811 PAGE: 17-29 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE

| type | location | description |
|----------|---------------|------------------|
| bridge | Cys-1 - Pen-9 | disulfide bridge |
| uncommon | Pen-9 | - |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| ===== | |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKYFSNIXW

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HITS AT: 1-10

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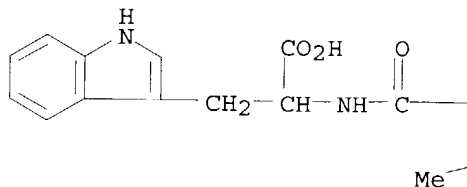
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LC STN Files: CA, CAPLUS, TOXCENTER

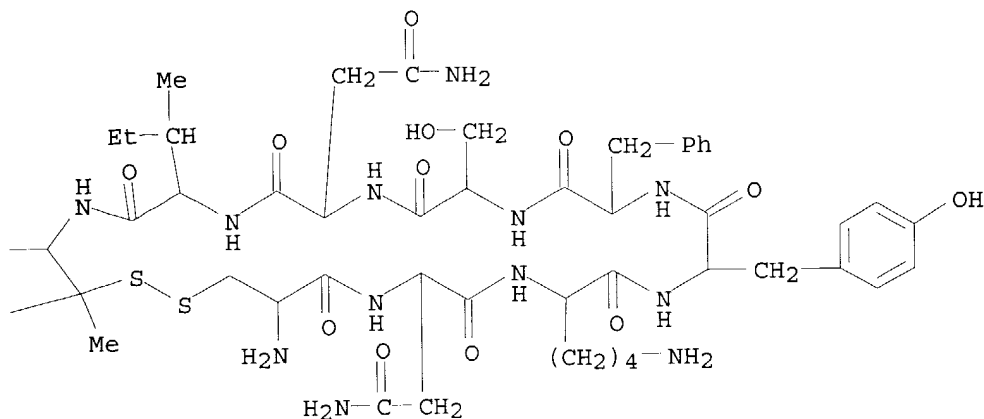
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP
(Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 10 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 321147-73-3 REGISTRY
 CN L-Tryptophan, D-cysteinyl-L-asparaginyl-N5-(aminocarbonyl)-L-ornithyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 18: PN: WO0105811 PAGE: 17-29 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE

| type | location | description |
|----------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| uncommon | Cit-3 | - |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNXYFSNICW
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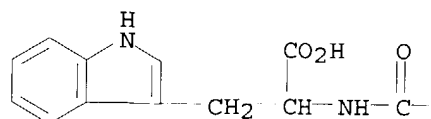
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 SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

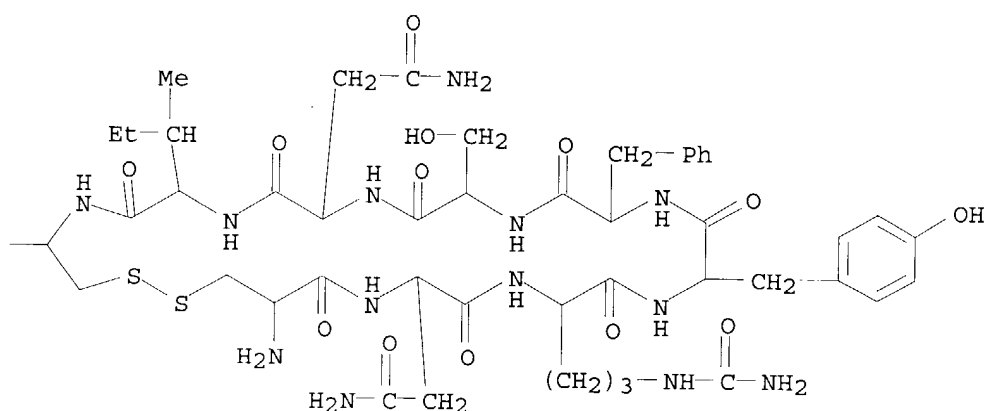
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 11 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-67-5 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-(2S)-2,4-diaminobutanoyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 15: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE

| type | ----- | location | ----- | description |
|----------|-------|----------|-------|------------------|
| bridge | Cys-1 | - | Cys-9 | disulfide bridge |
| uncommon | Dab-3 | - | - | - |

PATENT ANNOTATIONS (PNTE):

Sequence | Patent

Source | Reference

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Not Given | WO2001005811

| claimed PAGE

| 17-29

SEQ 1 CNXYFSNICW

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HITS AT: 1-10

MF C56 H74 N14 O15 S2

SR CA

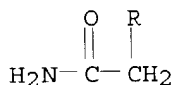
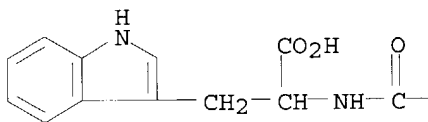
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

DT.CA Caplus document type: Journal; Patent

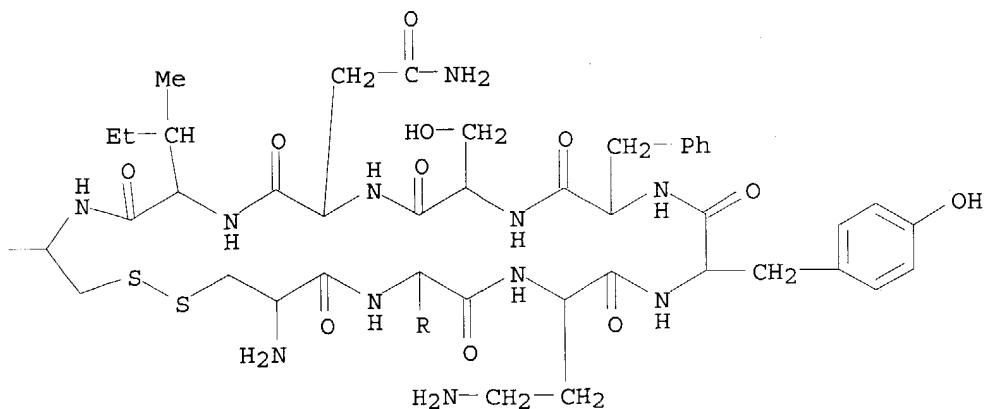
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 12 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 321147-65-3 REGISTRY
CN L-Tryptophan, D-cysteinyL-L-asparaginyL-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-.alpha.-aspartyl-L-isoleucyl-L-cysteinyL-, cyclic
(1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 14: PN: WO0105811 PAGE: 17-29 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE

| type | location | description |
|--------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |

PATENT ANNOTATIONS (PNTE):

| Sequence | Patent |
|-----------|---------------------------------------|
| Source | Reference |
| Not Given | WO2001005811 claimed PAGE 17-29 |

SEQ 1 CNKYFSDICW

HITS AT: 1-10

MF C58 H77 N13 O16 S2

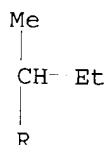
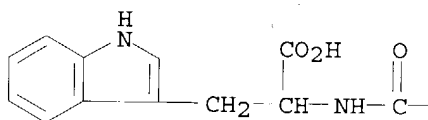
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LC STN Files: CA, CAPLUS, TOXCENTER

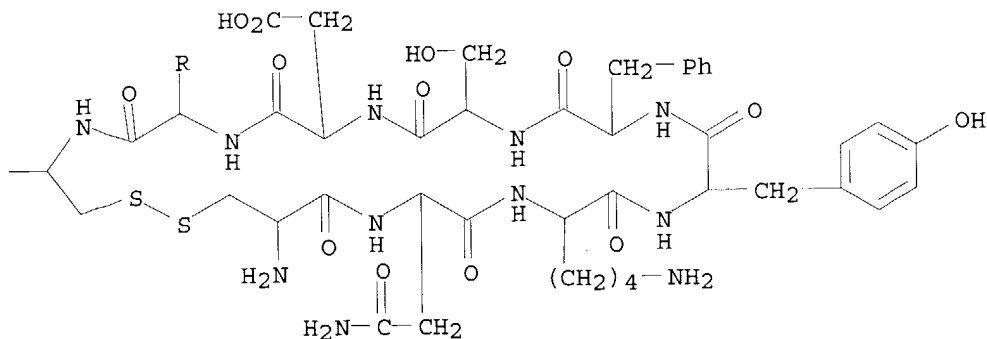
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 13 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 321147-61-9 REGISTRY
 CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-L-tyrosyl-3-(2-thienyl)-L-alanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic
 (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 12: PN: WO0105811 PAGE: 17-29 claimed protein
 FS PROTEIN SEQUENCE; STEREOSEARCH
 SQL 10
 NTE

| type | location | description |
|----------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| uncommon | Thi-5 - | - |

PATENT ANNOTATIONS (PNTE):

| Sequence | Patent |
|-----------|--------------|
| Source | Reference |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKYXSNICW
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HITS AT: 1-10

MF C56 H76 N14 O15 S3

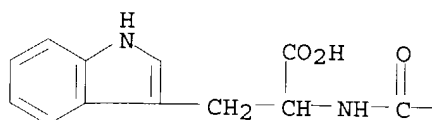
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LC STN Files: CA, CAPLUS, TOXCENTER

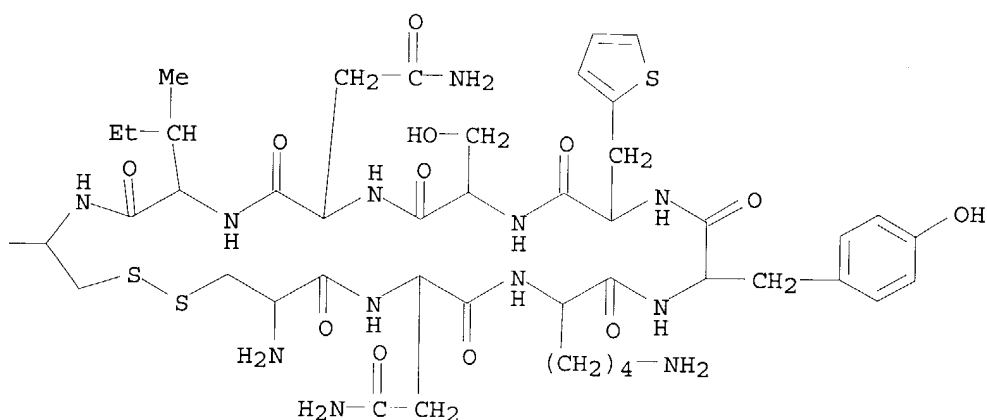
DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 14 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-59-5 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-histidyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 11: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE

| type | location | description |
|--------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |

PATENT ANNOTATIONS (PNTE):

Sequence | Patent

Source | Reference

=====+=====

Not Given | WO2001005811
| claimed PAGE
| 17-29

SEQ 1 CNHYFSNICW

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HITS AT: 1-10

MF C58 H73 N15 O15 S2

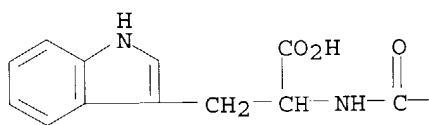
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LC STN Files: CA, CAPLUS, TOXCENTER

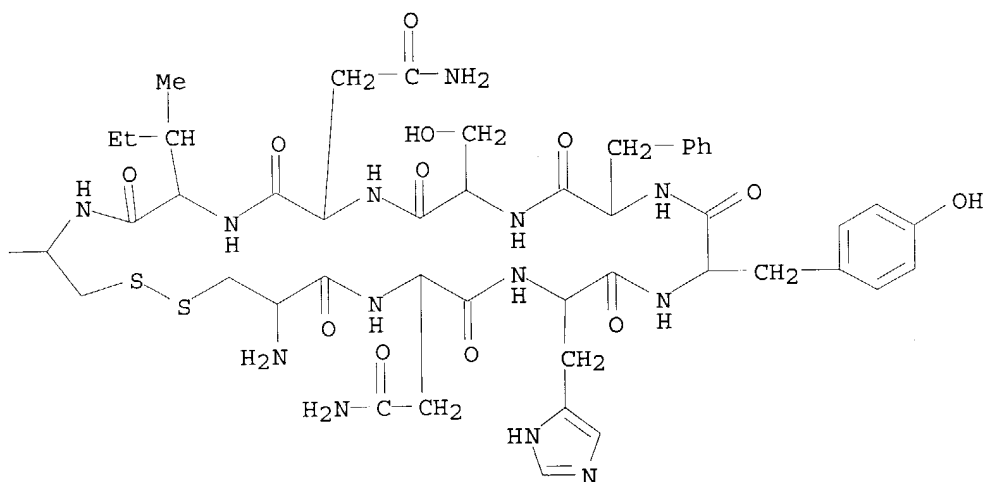
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 15 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-57-3 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-3-(2-thienyl)-L-alanyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 10: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE

| type | location | description |
|----------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| uncommon | Thi-4 | |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| ===== | |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKXFSNICW

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HITS AT: 1-10

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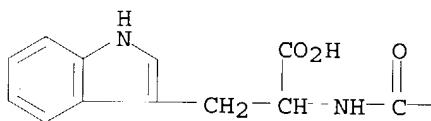
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LC STN Files: CA, CAPLUS, TOXCENTER

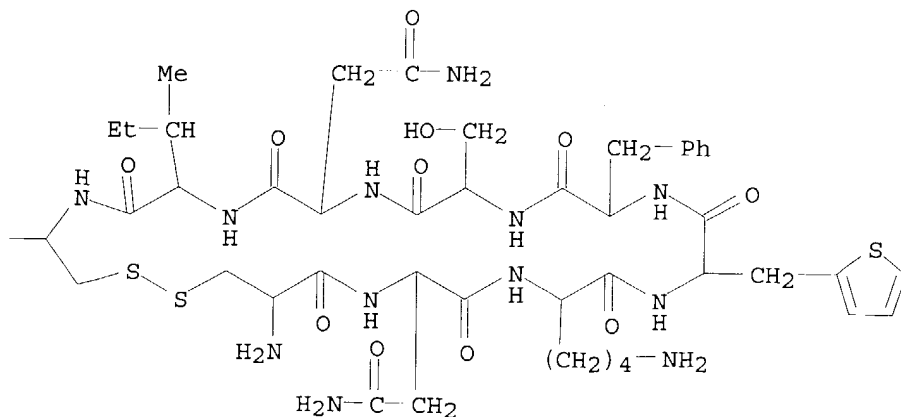
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 16 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN
RN 321147-49-3 REGISTRY
CN L-Tryptophan, D-cysteinyL-L-asparaginyL-3-amino-L-alanyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyL-L-isoleucyl-L-cysteinyL-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 6: PN: WO0105811 PAGE: 17-29 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE

| type | location | description |
|----------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |
| uncommon | Dpr-3 - | - |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNXYFSNICW

HITS AT: 1-10

MF C55 H72 N14 O15 S2

SR CA

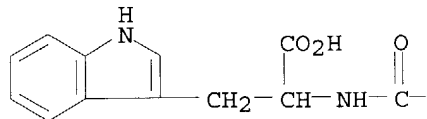
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

DT.CA Caplus document type: Journal; Patent

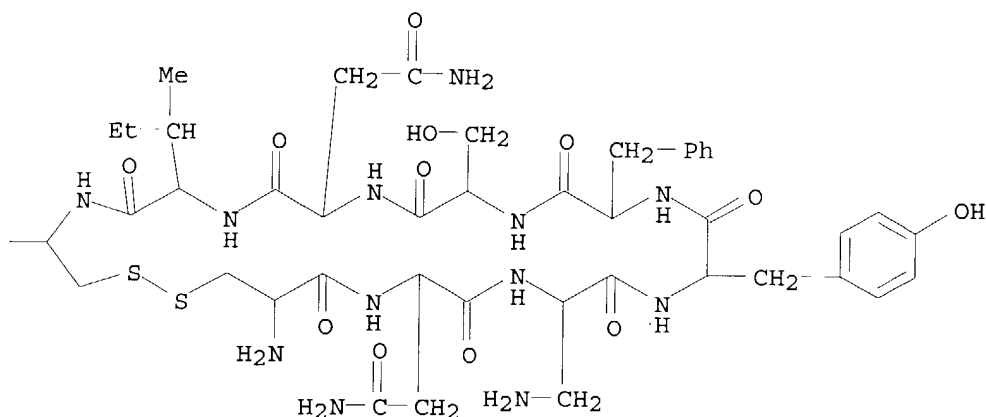
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 17 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-47-1 REGISTRY

CN L-Tryptophanamide, D-cysteinyl-L-asparaginyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 5: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE modified

| type | location | description |
|---------------|---------------|------------------|
| terminal mod. | Trp-10 | C-terminal amide |
| bridge | Cys-1 - Cys-9 | disulfide bridge |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKYFSNICW

HITS AT: 1-10

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MF C58 H79 N15 O14 S2

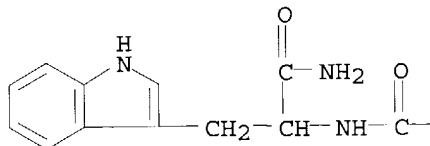
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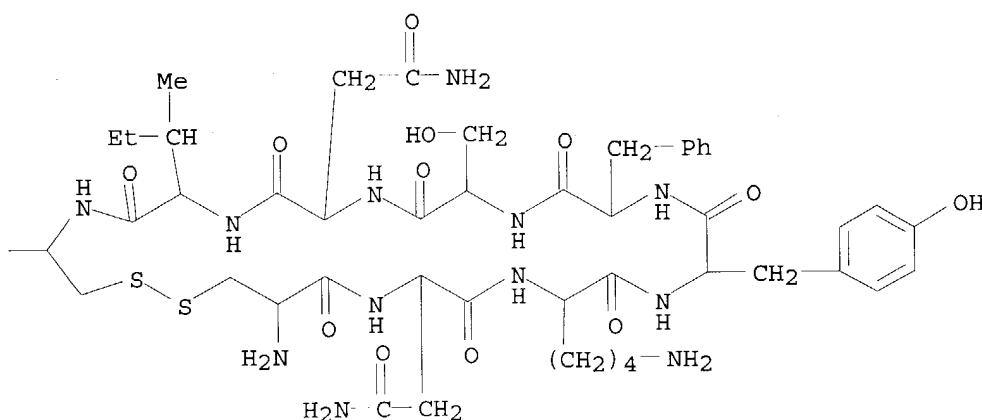
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 18 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 321147-43-7 REGISTRY

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1: PN: WO0105811 PAGE: 17-29 claimed protein

CN 3: PN: WO0105811 PAGE: 17-29 claimed protein

CN 4: PN: DE10209030 PAGE: 9 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE

| type | location | description |
|--------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |

PATENT ANNOTATIONS (PNTE):

Sequence | Patent

Source | Reference

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| | |
|-----------|--------------|
| Not Given | WO2001005811 |
| | claimed PAGE |

disulfide (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4: PN: WO0105811 PAGE: 17-29 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10

NTE

| type | location | description |
|--------|---------------|------------------|
| bridge | Cys-1 - Cys-9 | disulfide bridge |

PATENT ANNOTATIONS (PNTE):

| | |
|-----------|--------------|
| Sequence | Patent |
| Source | Reference |
| Not Given | WO2001005811 |
| | claimed PAGE |
| | 17-29 |

SEQ 1 CNKYFSNICW

HITS AT: 1-10

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MF C58 H78 N14 O15 S2

SR CA

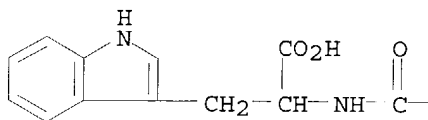
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

DT.CA Caplus document type: Journal; Patent

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RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

PAGE 1-A



|17-29

SEQ 1 CNKYFSNICW

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HITS AT: 1-10

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C58 H78 N14 O15 S2

SR CA

LC STN Files: CA, CAPLUS, CASREACT, PROUSDDR, TOXCENTER, USPATFULL

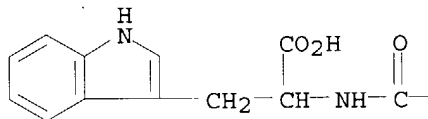
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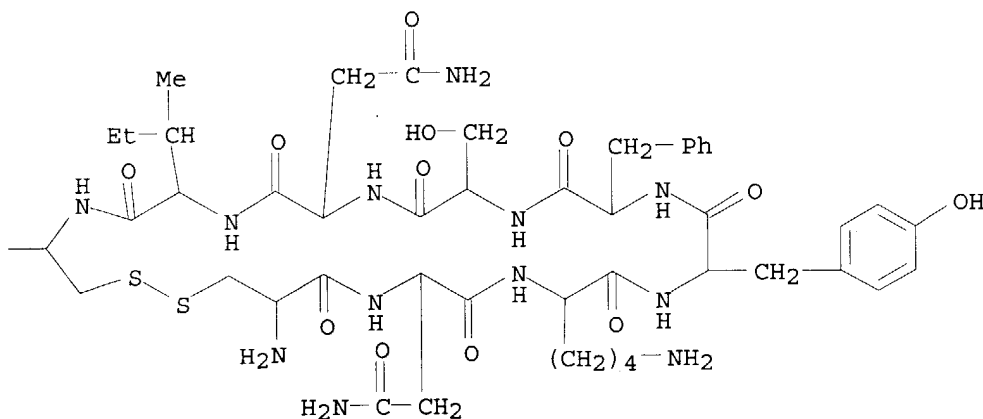
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RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 1-B



6 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 19 OF 19 REGISTRY COPYRIGHT 2004 ACS on STN

RN 214895-18-8 REGISTRY

CN L-Tryptophan, L-cysteinyl-L-asparaginyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.9) -

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
DE 19933701 A1 20010125 DE 1999-19933701 19990719
EP 1194531 A2 20020410 EP 2000-951406 20000719
EP 1194531 B1 20040512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
AT 266722 E 20040515 AT 2000-951406 20000719
PRIORITY APPLN. INFO.: DE 1999-19933701 A 19990719
WO 2000-EP6905 W 20000719
OTHER SOURCE(S): MARPAT 134:110477
ED Entered STN: 26 Jan 2001
AB Cyclic peptide compds. are provided which are used as inhibitors of
urokinase binding to urokinase receptors. The cyclic peptide compds. are
suitable for use as pharmaceutical active ingredients to combat diseases
which are mediated by urokinase and urokinase receptor.
IT 321147-43-7P 321147-49-3P 321147-67-5P
321147-91-5P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); PRP (Properties); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); PROC (Process); USES (Uses)
(cyclic peptidomimetic urokinase receptor antagonists and therapeutic
use)
IT 214895-18-8P 321147-47-1P 321147-57-3P
321147-59-5P 321147-61-9P 321147-65-3P
321147-73-3P 321147-75-5P 321147-77-7P
321147-79-9P 321147-81-3P 321147-83-5P
321147-87-9P 321147-93-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(cyclic peptidomimetic urokinase receptor antagonists and therapeutic
use)
IT 321147-43-7D, amino acid-substitution derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(cyclic peptidomimetic urokinase receptor antagonists and therapeutic
use)
L17 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:775656 CAPLUS
DOCUMENT NUMBER: 136:112295
TITLE: Cyclo19,31[D-Cys19]-uPA19-31 is a potent competitive
antagonist of the interaction of urokinase-type
plasminogen activator with its receptor (CD87)
AUTHOR(S): Magdolen, Viktor; Burgle, Markus; Arroyo De Prada,
Nuria; Schmiedeberg, Niko; Riemer, Christoph;
Schroeck, Florian; Kellermann, Josef; Degitz, Klaus;
Wilhelm, Olaf G.; Schmitt, Manfred; Kessler, Horst
CORPORATE SOURCE: Frauenklinik der Technischen Universitat Munchen,
Munchen, D-81675, Germany
SOURCE: Biological Chemistry (2001), 382(8), 1197-1205
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Oct 2001

AB Urokinase-type plasminogen activator (uPA) represents a central mol. in pericellular proteolysis and is implicated in a variety of physiol. and pathophysiol. processes such as tissue remodelling, wound healing, tumor invasion, and metastasis. UPA binds with high affinity to a specific cell surface receptor, uPAR (CD87), via a well defined sequence within the N-terminal region of uPA (uPA19-31). This interaction directs the proteolytic activity of uPA to the cell surface which represents an important step in tumor cell proliferation, invasion, and metastasis. Due to its fundamental role in these processes, the uPA/uPAR-system has emerged as a novel target for tumor therapy. Previously, we have identified a synthetic, cyclic, uPA-derived peptide, cyclo19,31uPA19-31, as a lead structure for the development of low mol. wt. uPA-analogs, capable of blocking uPA/uPAR-interaction. We now searched for peptide variants of cyclo19,31uPA19-31 with elevated affinities for uPAR binding. Among other tasks, we performed a systematic D-amino acid scan of uPA19-31, in which each of the 13 L-amino acids was individually substituted by the corresponding D-amino acid. This led to the identification of cyclo19,31[D-Cys19]-uPA19-31 as a potent inhibitor of uPA/uPAR-interaction, displaying only a 20 to 40-fold lower binding capacity as compared to the naturally occurring uPAR-ligands uPA and its amino-terminal fragment. Cyclo19,31[D-Cys19]-uPA19-31 not only blocks binding of uPA to uPAR but is also capable of efficiently displacing uPAR-bound uPA from the cell surface and to inhibit uPA-mediated, tumor cell-assocd. plasminogen activation and fibrin degrdn. Thus, cyclo19,31[D-Cys19]-uPA19-31 represents a promising therapeutic agent to significantly affect the tumor-assocd. uPA/uPAR-system.

IT 390391-14-7

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(cyclo19,31[D-Cys19]-uPA19-31 is a potent competitive antagonist of the interaction of urokinase-type plasminogen activator with its receptor (CD87))

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1998:716166 CAPLUS

DOCUMENT NUMBER: 129:310886

TITLE: Peptide inhibitors of the urokinase receptor

INVENTOR(S): Kessler, Horst; Graeff, Heinrich; Schmitt, Manfred; Magdolen, Viktor; Wilhelm, Olaf G.; Riemer, Christoph; Buergle, Markus

PATENT ASSIGNEE(S): Wilex Biotechnology G.m.b.H., Germany

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|--|----------|-----------------|----------|
| WO 9846632 | A2 | 19981022 | WO 1998-EP2179 | 19980414 |
| WO 9846632 | A3 | 19990128 | | |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |

AU 9872164 A1 19981111 AU 1998-72164 19980414
AU 730333 B2 20010301
EP 971948 A2 20000119 EP 1998-919267 19980414
EP 971948 B1 20030813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
JP 2001519823 T2 20011023 JP 1998-543493 19980414
AT 247130 E 20030815 AT 1998-919267 19980414
MX 9909109 A 20000731 MX 1999-9109 19991005
US 2004138110 A1 20040715 US 2004-756289 20040114
PRIORITY APPLN. INFO.: EP 1997-106024 A 19970411
WO 1998-EP2179 W 19980414
US 2000-402464 A3 20000107

OTHER SOURCE(S): MARPAT 129:310886

ED Entered STN: 11 Nov 1998

AB Disclosed are peptides as agents for inhibiting urokinase binding to its receptor. Said peptides, preferably cyclical, are suitable as active agents for treating diseases involving urokinase or the receptor thereof, e.g., tumor metastasis.

IT **214895-18-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(peptide inhibitors of the urokinase receptor)

L17 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:240998 CAPLUS

DOCUMENT NUMBER: 138:265592

TITLE: Method for the determination of protein protein interactions by fluorescence measurement

INVENTOR(S): Burgle, Markus; Guthaus, Elke; Schmitt, Manfred; Magdolen, Viktor; Kessler, Horst

PATENT ASSIGNEE(S): Willex AG, Germany

SOURCE: Ger. Offen., 6 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|------------------|-------------|
| DE 10209030 | A1 | 20030327 | DE 2002-10209030 | 20020301 |
| | | | DE 2001-10143768 | IA 20010906 |

PRIORITY APPLN. INFO.:

ED Entered STN: 28 Mar 2003

AB The invention provides a method for the detn. of interactions, in particular protein-protein interactions, by means of fluorescence measurements, as well as suitable reagents and kits. The method is in particular suitable for detg. the influence of test substances on interactions, for example in screening processes for the identification of therapeutic active substances, or for the identification and characterization of new receptor ligands or receptors from biol. samples.

IT **321147-43-7 321147-87-9**

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(protein-protein interaction detn. by fluorescence measurement)

L17 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:158090 CAPLUS

DOCUMENT NUMBER: 136:212777

TITLE: Urokinase antagonist cyclic peptide structure mimetics and application to drug design

INVENTOR(S): Wilhelm, Olaf; Buergle, Markus; Kessler, Horst;
Schmiedeberg, Niko
PATENT ASSIGNEE(S): Willex A.-G., Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002016929 | A2 | 20020228 | WO 2001-EP9668 | 20010821 |
| WO 2002016929 | A3 | 20021010 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2002012145 | A5 | 20020304 | AU 2002-12145 | 20010821 |
| EP 1311856 | A2 | 20030521 | EP 2001-980255 | 20010821 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| US 2003232389 | A1 | 20031218 | US 2003-362184 | 20030221 |
| PRIORITY APPLN. INFO.: | | | EP 2000-118099 | A 20000823 |
| | | | WO 2001-EP9668 | W 20010821 |

ED Entered STN: 01 Mar 2002

AB The NMR structure of the peptidic urokinase type plasminogen activator antagonist cyclo[21,29][D-Cys21Cys29]-uPA21-30 (cyclo[1,9]D-Cys-Asn-Lys-Tyr-Phe-Ser-Asn-Ile-Cys-Trp) has been solved to identify design strategies for peptidomimetics that interfere with the binding of urokinase type plasminogen activator with its receptor.

IT **321147-43-7**

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urokinase antagonist cyclic peptide structure mimetics and application to drug design)

L17 ANSWER 9 OF 11 USPATFULL on STN

ACCESSION NUMBER: 2003:330178 USPATFULL

TITLE: Urokinase peptide structure mimetics

INVENTOR(S): Wilhelm, Olaf G, UNITED STATES

Burgle, Markus, M?uuml;nchen, GERMANY, FEDERAL REPUBLIC OF
Kessler, Horst, Schwalbach, GERMANY, FEDERAL REPUBLIC OF
Schmiedeberg, Niko, Rhein, GERMANY, FEDERAL REPUBLIC OF

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2003232389 | A1 | 20031218 |
| APPLICATION INFO.: | US 2003-362184 | A1 | 20030221 (10) |
| | WO 2001-EP9668 | | 20010821 |

| | NUMBER | DATE |
|-----------------------|----------------|----------|
| PRIORITY INFORMATION: | EP 2000-118099 | 20000823 |
| DOCUMENT TYPE: | Utility | |

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROTHWELL, FIGG, ERNST & MANBECK, P.C., 1425 K STREET,
N.W., SUITE 800, WASHINGTON, DC, 20005
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 866

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The NMR structure of the peptidic urokinase type plasminogen activator antagonist cyclo[21,29] [D-Cys21Cys29]-uPA.sub.21-30 has been solved to identify design strategies for peptidomimetics that interfere with the binding of urokinase type plasminogen activator with its receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

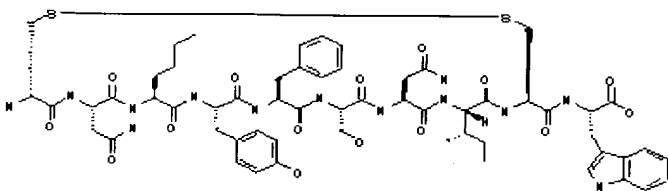
IT **321147-43-7**

(urokinase antagonist cyclic peptide structure mimetics and application to drug design)

L17 ANSWER 10 OF 11 PROUSDDR COPYRIGHT 2004 PROUS SCIENCE on STN

ACCESSION NUMBER: 2003:906 PROUSDDR
DOCUMENT NUMBER: 328089
CHEMICAL NAME: Cyclo(21-29) (D-Cys21,L-Nle23,L-Cys29)uPA(21-30)
CHEMICAL NAME: D-Cysteinyl-L-asparaginyl-L-norleucyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-L-tryptophan cyclic disulfide
DRUG NAME: WX-360-Nle
CAS REGISTRY NUMBER: **321147-91-5**
MOLECULAR FORMULA: C58 H77 N13 O15 S2
HIGHEST DEV. PHASE: PRECLINICAL
ORIGINATOR: Wilex
CLASSIFICATION CODE: Oncolytic Drugs
OTHER SOURCE: PROUSDDR 2003000057 (DDR Preferred)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 9 May 2004

STRUCTURE:



PROUS REFERENCES:

RefID: 706608 (Text Available)
Drug Data Report, Vol. 25, No. 1, pp 84, 2003

REFERENCE TEXT:

RefID: 706608
ACTION - Antineoplastic and antimetastatic agent, a urokinase-derived cyclic peptide shown to inhibit the urokinase plasminogen activator (uPA)/uPA receptor interaction (IC₅₀ = 60 nM). The peptide is resistant to proteolytic cleavage and is stable in blood serum or plasma; it significantly inhibited endothelial cell assembly in rat aortic rings and exhibited low cell toxicity. In mice bearing human ovarian cancer cells,

the peptide administered i.p. at a dose of 20 mg/kg for 37 days significantly reduced tumor weight and spread into peritoneum. Another related compound is:

PATENT REFERENCES:

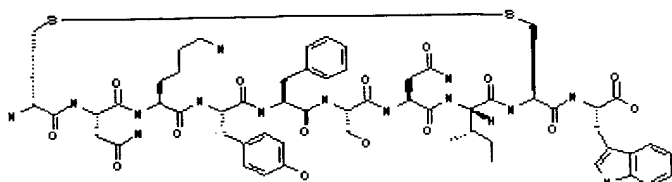
TITLE: Cyclic peptidomimetic urokinase receptor antagonists
INVENTOR(S): Kessler, H.; Wilhelm, O.; Burgle, M.; Potthoff, N.; Schmiedeberg, N.
PATENT ASSIGNEE(S): Wilex
PATENT INFORMATION: DE 19933701 20010125
WO 2001005811 20010125
PRIORITY INFORMATION: DE 1999-33701 19990719

REFERENCES:

- (1) RefID: 700044, Periodic Publication
"Synthesis, solution structure, and biological evaluation of urokinase type plasminogen activator (uPA)-derived receptor binding domain mimetics"
Schmiedeberg, N.; Schmitt, M.; Rolz, C.; et al., J Med Chem, Vol. 45, No. 23, pp 4984, 2002
- (2) RefID: 705858, Periodic Publication
"High-affinity urokinase-derived cyclic peptides inhibiting urokinase/urokinase receptor-interaction: Effects on tumor growth and spread"
Sato, S.; Kopitz, C.; Scmalix, W.A.; Muehlenweg, B.; Kessler, H.; Schmitt, M.; Kruger, A.; Magdolen, V., FEBS Lett, Vol. 528, No. 1-3, pp 212, 2002

L17 ANSWER 11 OF 11 PROUSDDR COPYRIGHT 2004 PROUS SCIENCE on STN
ACCESSION NUMBER: 2003:57 PROUSDDR
DOCUMENT NUMBER: 301479
CHEMICAL NAME: Cyclo(21-29) (D-Cys21,L-Cys29)uPA(21-30)
CHEMICAL NAME: D-CysteinyL-L-asparaginyL-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyL-L-isoleucyl-L-cysteinyL-L-tryptophan cyclic disulfide
DRUG NAME: WX-360
CAS REGISTRY NUMBER: 321147-43-7
MOLECULAR FORMULA: C58 H78 N14 O15 S2
STATUS: Actively Investigated
HIGHEST DEV. PHASE: PRECLINICAL
ORIGINATOR: Wilex
CLASSIFICATION CODE: Oncolytic Drugs
ACTION MECHANISM: Angiogenesis Inhibitors
OTHER SOURCE: PROUSDDR 2003000906 (DDR Nonpreferred)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 9 May 2004

STRUCTURE:



Drug Data Report, Vol. 25, No. 1, pp 84, 2003

REFERENCE TEXT: RefID: 706608
ACTION - Antineoplastic and antimetastatic agent, a urokinase-derived cyclic peptide shown to inhibit the urokinase plasminogen activator (uPA)/uPA receptor interaction (IC50 = 60 nM). The peptide is resistant to proteolytic cleavage and is stable in blood serum or plasma; it significantly inhibited endothelial cell assembly in rat aortic rings and exhibited low cell toxicity. In mice bearing human ovarian cancer cells, the peptide administered i.p. at a dose of 20 mg/kg for 37 days significantly reduced tumor weight and spread into peritoneum. Another related compound is:

PATENT REFERENCES:

TITLE: Cyclic peptidomimetic urokinase receptor antagonists
INVENTOR(S): Kessler, H.; Wilhelm, O.; Burgle, M.; Potthoff, N.; Schmiedeberg, N.
PATENT ASSIGNEE(S): Wilex
PATENT INFORMATION: DE 19933701 20010125
WO 2001005811 20010125
PRIORITY INFORMATION: DE 1999-33701 19990719

TITLE: Urokinase peptide structure mimetics
INVENTOR(S): Kessler, H.; Wilhelm, O.; Burgle, M.; Schmiedeberg, N.
PATENT ASSIGNEE(S): Wilex
PATENT INFORMATION: WO 2002016929 20020228
PRIORITY INFORMATION: EP 2000-118099 20000823

REFERENCES:

- (1) RefID: 620433, Congress Literature
"Inhibitors of the urokinase-type plasminogen activator system as potent candidates of novel anticancer therapeutics"
Probst, J.C.; et al., Angiogenesis Cancer: Basic Mech Ther Appl, Oct 11 2000-Oct 15 2000, Traverse City, (Abst B21)
- (2) RefID: 611534, Periodic Publication
"Small molecule approach to inhibit the urokinase-type plasminogen activator system"
Probst, J.C.; Burgle, M.; Foekens, J.; et al., Proc Am Assoc Cancer Res, Vol. 42, (Abst 370), 2001
- (3) RefID: 663198, Periodic Publication
"Inhibitors of the urokinase-type plasminogen activator system"
Wosikowski, K.; Foekens, J.; Kopitz, C.; et al., Proc Am Assoc Cancer Res, Vol. 43, (Abst 791), 2002
- (4) RefID: 700044, Periodic Publication
"Synthesis, solution structure, and biological evaluation of urokinase type plasminogen activator (uPA)-derived receptor binding domain mimetics"
Schmiedeberg, N.; Schmitt, M.; Rolz, C.; et al., J Med Chem, Vol. 45, No. 23, pp 4984, 2002
- (5) RefID: 705858, Periodic Publication
"High-affinity urokinase-derived cyclic peptides inhibiting urokinase/urokinase receptor-interaction: Effects on tumor growth and spread"
Sato, S.; Kopitz, C.; Scmalix, W.A.; Muehlenweg, B.; Kessler, H.; Schmitt, M.; Kruger, A.; Magdolen, V., FEBS Lett, Vol. 528, No. 1-3, pp

212, 2002

- (6) RefID: 705859, Periodic Publication
"uPA-silica-Particles (SP-uPA): A novel analytical system to
investigate uPA-uPAR interaction and to test synthetic uPAR antagonists
as potential cancer therapeutics"
Guthaus, E.; Burtle, M.; Schmiedeberg, N.; et al., Biol Chem, Vol. 383,
No. 1, pp 207, 2002

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DICTIONARY FILE UPDATES: 27 SEP 2004 HIGHEST RN 752974-11-1

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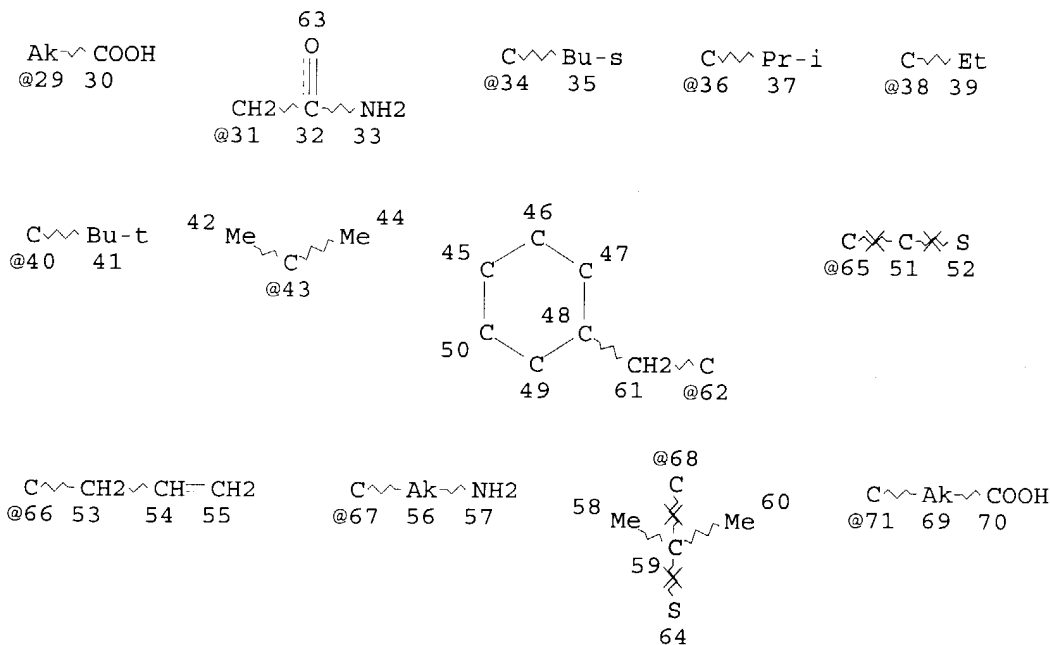
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Experimental and calculated property data are now available. For more
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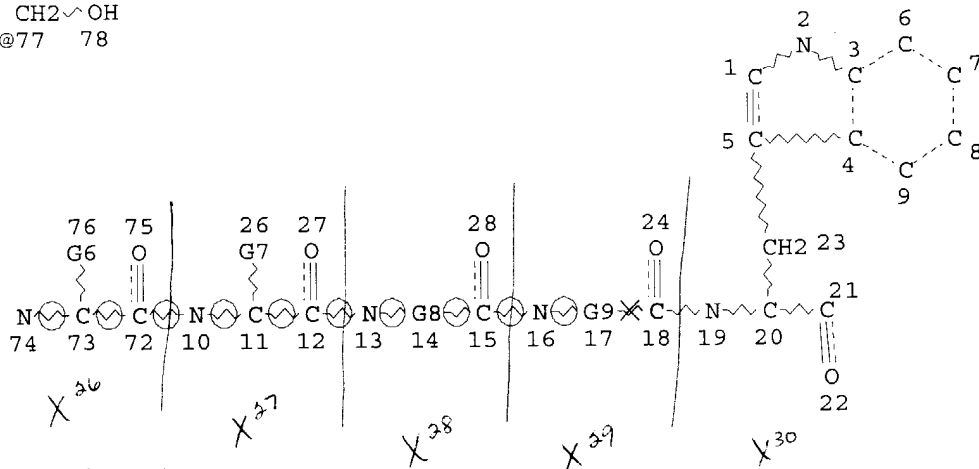
L1

STR



Page 1-A

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Page 2-A

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VAR G7=29/31

VAR G8=34/36/62/38/40/43

VAR G9=65/71/66/67/68

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CONNECT IS E2 RC AT 56

CONNECT IS E2 RC AT 69

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 77

STEREO ATTRIBUTES: NONE

L3 28 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 3313 ITERATIONS

SEARCH TIME: 00.00.03

= ring bonds & nodes

= ring or chain bond & node

Note: entire structure was too large to draw (exceeded Registry file limits), so only a portion was drawn. All amino acids (common & uncommon) listed by applicants are included in query

28 ANSWERS

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FILE 'TOXCENTER' ENTERED AT 09:40:20 ON 28 SEP 2004

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FILE 'PROUSDDR' ENTERED AT 09:40:20 ON 28 SEP 2004

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L5 18 L3

=> dup rem 15

DUPLICATE IS NOT AVAILABLE IN 'PROUSDDR'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L5

L6 12 DUP REM L5 (6 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE CAPLUS
ANSWER '10' FROM FILE USPATFULL
ANSWERS '11-12' FROM FILE PROUSSDDR

=> d ibib ed abs hitstr 1-10; d iall 11-12

L6 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:329815 CAPLUS

DOCUMENT NUMBER: 139:270566

TITLE: Protease inhibitors prevent plasminogen-mediated, but
not pemphigus vulgaris-induced, acantholysis in human
epidermis

AUTHOR(S): Schuh, Theda; Besch, Robert; Braungart, Evelyn; Flaig,
Michael J.; Douwes, Kathrin; Sander, Christian A.;
Magdolen, Viktor; Probst, Christopher; Wosikowski,
Katja; Degitz, Klaus

CORPORATE SOURCE: Department of Dermatology, Ludwig-Maximilians
University, Munich, D-80337, Germany

SOURCE: Biological Chemistry (2003), 384(2), 311-315
CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER: Walter de Gruyter GmbH & Co. KG

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 30 Apr 2003

AB Pemphigus is an autoimmune blistering disease of the skin and mucous
membranes. It is caused by autoantibodies directed against desmosomes,
which are the principal adhesion structures between epidermal
keratinocytes. Binding of autoantibodies leads to the destruction of
desmosomes resulting in the loss of cell-cell adhesion (acantholysis) and
epidermal blisters. The plasminogen activator system has been implicated
as a proteolytic effector in pemphigus. We have tested inhibitors of the
plasminogen activator system with regard to their potential to prevent
pemphigus-induced cutaneous pathol. In a human split skin culture system,
IgG preps. of sera from pemphigus vulgaris patients caused histopathol.
changes (acantholysis) similar to those obsd. in the original pemphigus
disease. All inhibitors that were tested (active site inhibitors directed
against uPA, tPA, and/or plasmin; antibodies neutralizing the enzymic
activity of uPA or tPA; substances interfering with the binding of uPA to
its specific cell surface receptor uPAR) failed to prevent pemphigus
vulgaris IgG-mediated acantholysis. Plasminogen-mediated acantholysis,
however, was effectively antagonized by the synthetic active site serine
protease inhibitor WX-UK1 or by p-aminomethylbenzoic acid. Our data argue
against applying anti-plasminogen activator/anti-plasmin strategies in the
management of pemphigus.

IT 321147-63-1

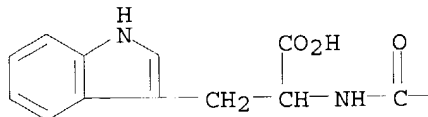
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(protease inhibitors prevent plasminogen-mediated, but not pemphigus
vulgaris-induced, acantholysis in human epidermis)

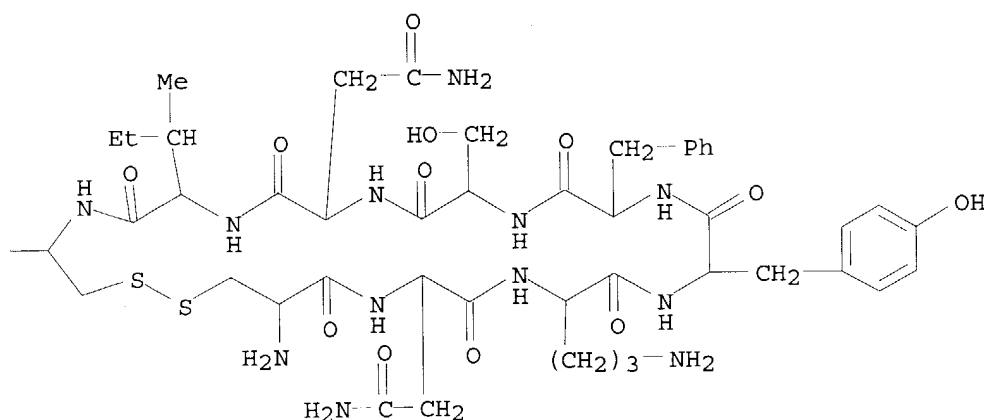
RN 321147-63-1 CAPLUS

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-ornithyl-L-tyrosyl-L-
phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic
(1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:760726 CAPLUS
DOCUMENT NUMBER: 138:4806
TITLE: Synthesis, Solution Structure, and Biological Evaluation of Urokinase Type Plasminogen Activator (uPA)-Derived Receptor Binding Domain Mimetics
AUTHOR(S): Schmiedeberg, Niko; Schmitt, Manfred; Roelz, Christian; Truffault, Vincent; Sukopp, Martin; Buergle, Markus; Wilhelm, Olaf G.; Schmalix, Wolfgang; Magdolen, Viktor; Kessler, Horst
CORPORATE SOURCE: Institut fuer Organische Chemie und Biochemie, Technische Universitaet Muenchen, Garching, D-85747, Germany
SOURCE: Journal of Medicinal Chemistry (2002), 45(23), 4984-4994
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:4806
ED Entered STN: 08 Oct 2002
AB Tumor cell migration and metastasis in cancer are facilitated by interaction of the serine protease urokinase type plasminogen activator (uPA) with its receptor uPAR (CD 87). Over-expression of uPA and uPAR in

cancer tissues is assocd. with a high incidence of disease recurrence and early death. In agreement with these findings, disruption of the protein-protein interaction between uPAR present on tumor cells and its ligand uPA evolved as an attractive intervention strategy to impair tumor growth and metastasis. For this, the uPAR antagonist cyclo[19,31] [D-Cys19]-uPA19-31 was optimized to efficiently interrupt binding of uPA to cellular uPAR. First, the disulfide bridge of this lead peptide was shifted, and then, the modified peptide was shortened from the amino and carboxy terminus to generate cyclo[21,29] [Cys21,29]-uPA21-30. Next, cyclo[21,29] [D-Cys21Cys29]-uPA21-30 was yielded by changing the chirality of Cys21 to D-Cys21. For anal. of uPAR binding activity, the authors employed competitive flow cytofluorometric receptor binding assays, using FITC-uPA as the ligand and U937 promyeloid leukemia cells as the cellular source of uPAR. As demonstrated for cyclo[21,29] [D-Cys21Cys29]-uPA21-30, the achieved peptide modifications maintained receptor binding activity ($IC_{50} = 0.04 \mu M$), which is close in order to that of the parent protein ligand, uPA ($IC_{50} = 0.01 \mu M$). A detailed NMR anal. with restrained and free mol. dynamics calcns. in explicit H₂O exhibits a well-defined structure with characteristic features such as an ω -loop with two β -turns about Lys3, Tyr4, Ser6, and Asn7. Hydrophobic clustering of the side chains of Tyr4, Phe5, Ile8, and Trp10 is obsd. Side chain mobility is analyzed with time-dependent distance restraints. The NMR structure of cyclo[21,29] [D-Cys21Cys29]-uPA21-30 is very similar to the previously reported structure of the amino terminal fragment of uPA. Systematic point mutations led to cyclo[21,29] [D-Cys21Nle23Cys29]-uPA21-30, which still binds to uPAR but is resistant to proteolytic cleavage, e.g., by the tumor-assocd. serine proteases uPA and plasmin, and is stable in blood serum or plasma. In conclusion, small cyclic peptides were created, which mimic the structure and activity of the binding epitope of uPA to uPAR and which may serve as novel therapeutic agents in cancer metastasis.

IT 214895-18-8P 321147-43-7P 321147-49-3P

321147-63-1P 321147-67-5P 321147-91-5P

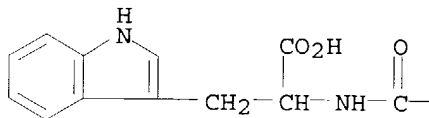
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn., soln. structure, and biol. evaluation of cyclic peptides that interfere with the binding of urokinase type plasminogen activator (uPA) with its receptor (uPAR))

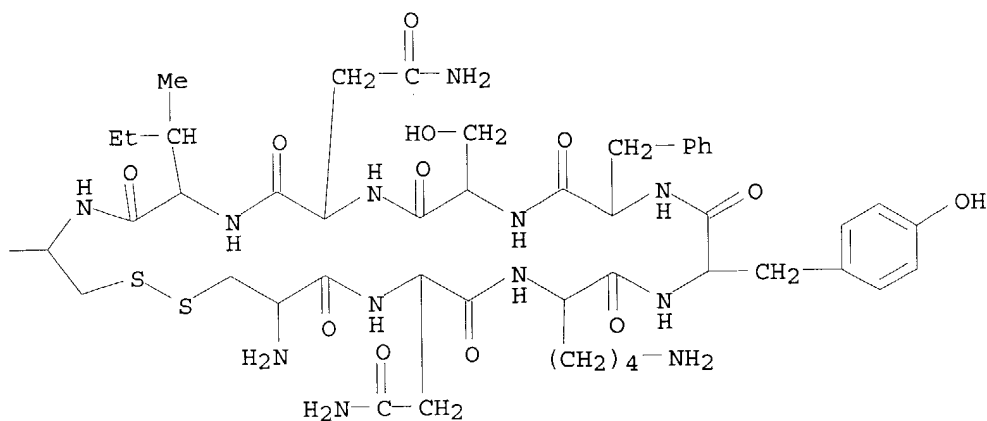
RN 214895-18-8 CAPLUS

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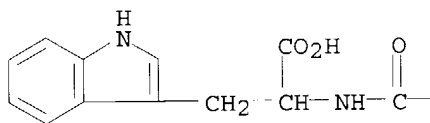


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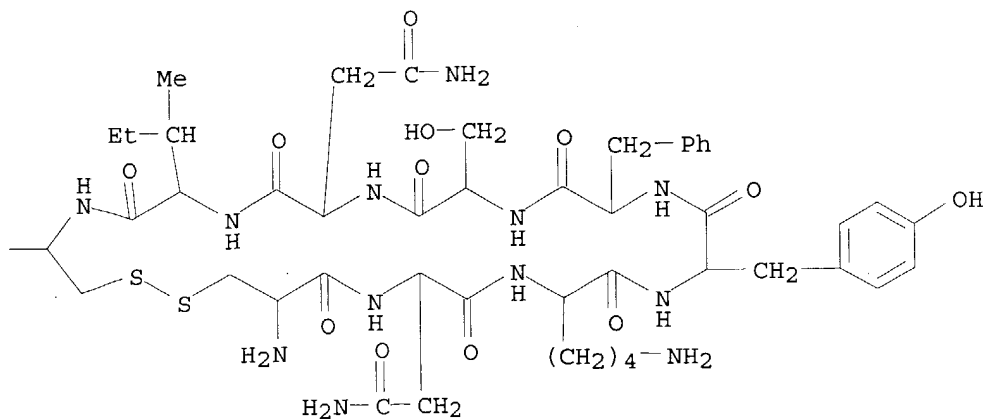


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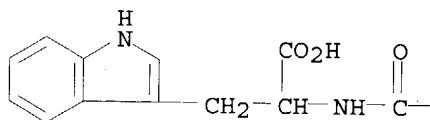
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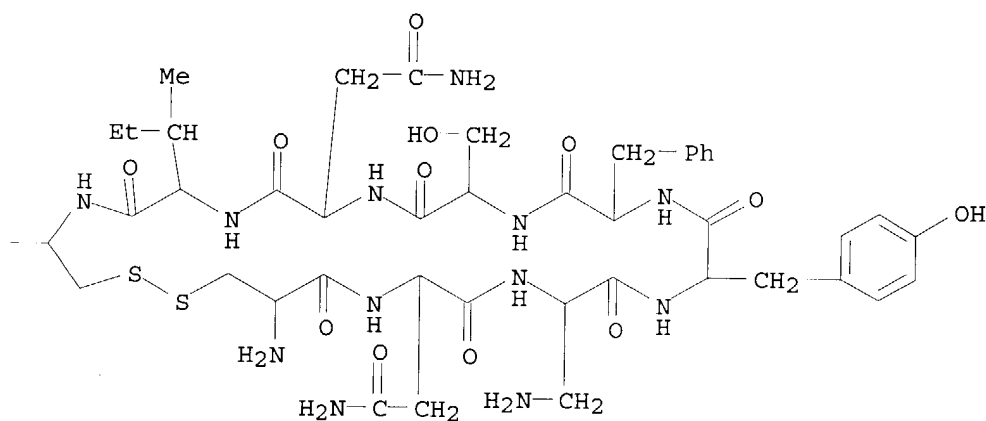
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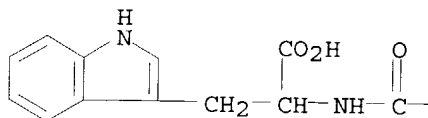


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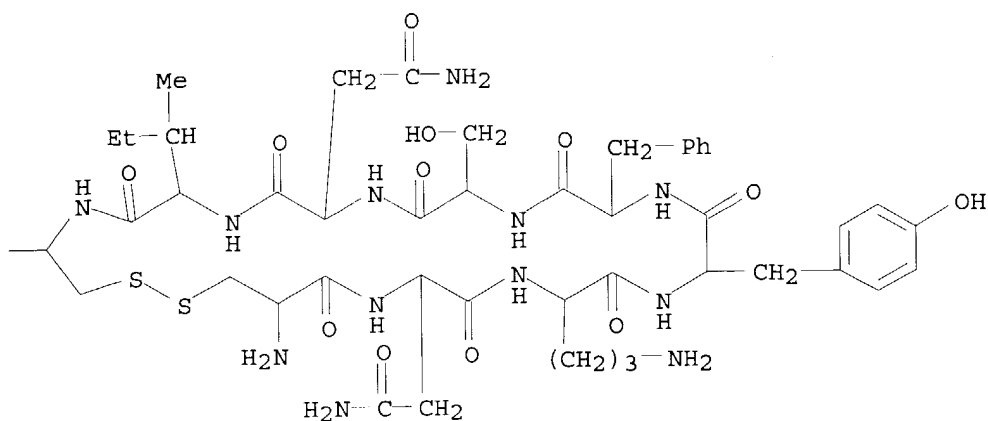


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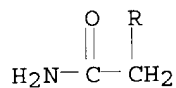
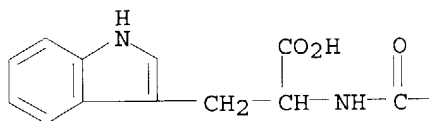


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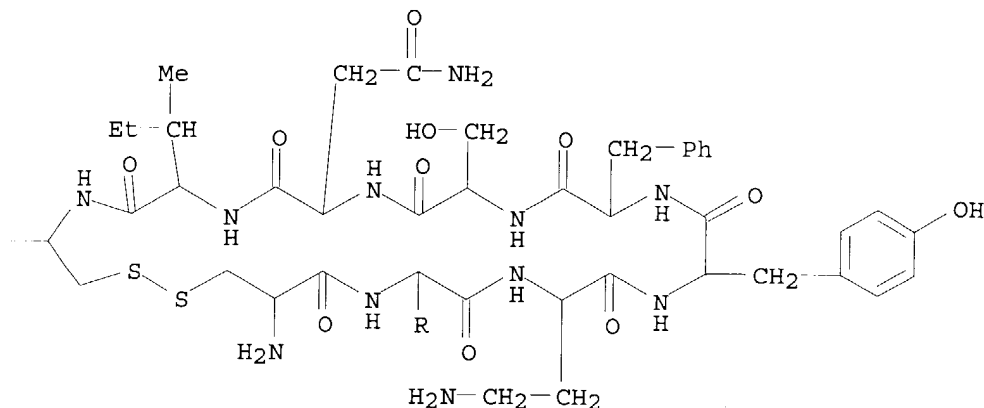


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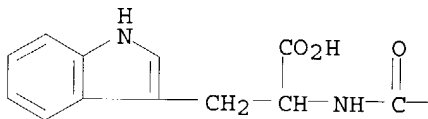


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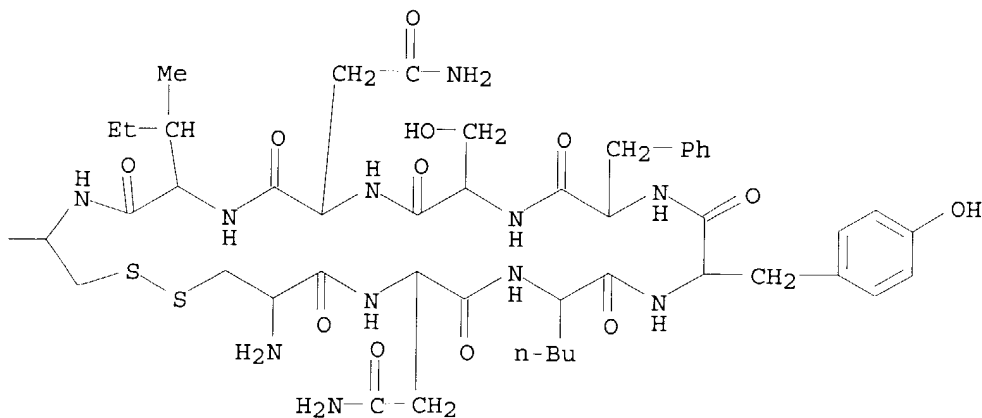


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REFERENCE COUNT:

46

THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:726694 CAPLUS

DOCUMENT NUMBER: 138:314033

TITLE: High-affinity urokinase-derived cyclic peptides
inhibiting urokinase/urokinase receptor-interaction:
effects on tumor growth and spread

AUTHOR(S): Sato, Sumito; Kopitz, Charlotte; Schmalix, Wolfgang
A.; Muehlenweg, Bernd; Kessler, Horst; Schmitt,
Manfred; Kruger, Achim; Magdolen, Viktor

CORPORATE SOURCE: Klinikum rechts der Isar, Klinische Forschergruppe der
Frauenklinik, Technische Universitat Munchen, Munchen,
D-81675, Germany

SOURCE: FEBS Letters (2002), 528(1-3), 212-216

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 25 Sep 2002

AB Urokinase-type plasminogen activator (uPA) binds with high affinity to its
specific cell surface receptor (uPAR) (CD87) via a well-defined sequence
within the N-terminal region of uPA (uPA19-31). Since this
uPA/uPAR-interaction plays a significant role in tumor cell invasion and
metastasis, it has become an attractive therapeutic target. Two small
peptidic cyclic competitive antagonists of uPA/uPAR-interaction have been
developed, based on the uPAR binding site in uPA: WX-360
(cyclo21,29[D-Cys21]-uPA21-30[S21C;H29C]) and its norleucine (Nle) deriv.
WX-360-Nle (cyclo21,29[D-Cys21]-uPA21-30[S21C;K23Nle;H29C]). These
peptides display an only five to 10-fold lower affinity to uPAR as
compared to the naturally occurring uPAR-ligand uPA. In this study,
WX-360 and WX-360-Nle were tested in nude mice for their potency to
inhibit tumor growth and i.p. spread of lacZ-tagged human ovarian cancer
cells. I.p. administration of either cyclic peptide (20 mg peptide/kg;
1.times. daily for 37 days) into the tumor-bearing nude mice resulted in a
significant redn. of tumor wt. and spread within the peritoneum as
compared to the untreated control group. This is the first report
demonstrating effective redn. of tumor growth and spread of human ovarian
cancer cells in vivo by small synthetic uPA-derived cyclic peptides
competitively interfering with uPA/uPAR-interaction. Thus, both WX-360
and WX-360-Nle are promising novel compds. to reduce dissemination of
human ovarian carcinoma.

IT 321147-43-7 321147-91-5

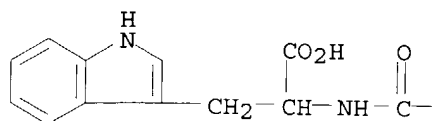
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)

(high-affinity urokinase-derived cyclic peptides inhibiting
urokinase/urokinase receptor-interaction and effects on tumor growth
and spread)

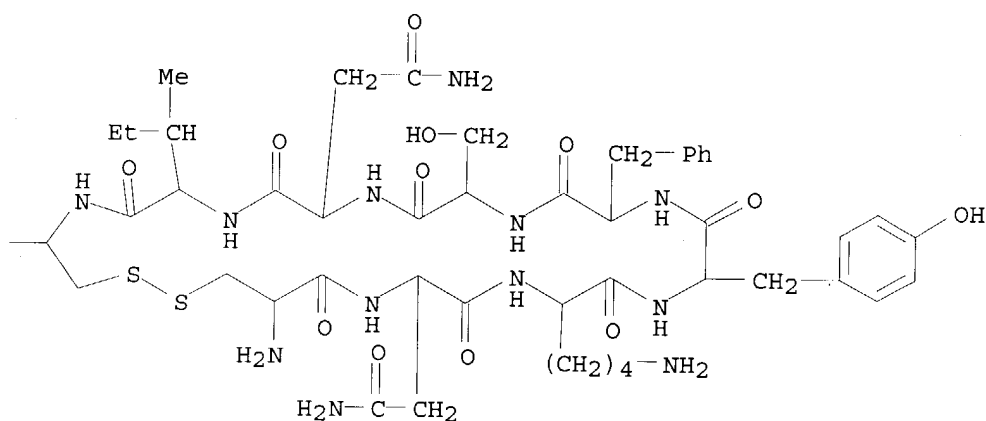
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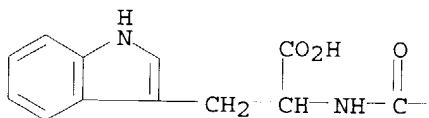


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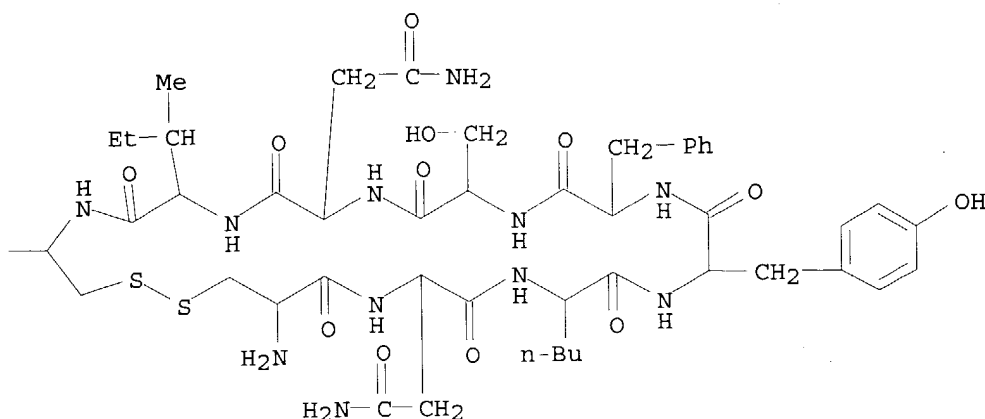


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REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2002:289240 CAPLUS

DOCUMENT NUMBER: 137:257163

TITLE: uPA-silica-particles (SP-uPA): a novel analytical system to investigate uPA-uPAR interaction and to test synthetic uPAR antagonists as potential cancer therapeutics

AUTHOR(S): Guthaus, Elke; Burtle, Markus; Schmiedeberg, Niko; Hocke, Stefan; Eickler, Alexandra; Kramer, Michael D.; Sweep, C. G. J. Fred; Magdolen, Viktor; Kessler, Horst; Schmitt, Manfred

CORPORATE SOURCE: Klinische Forschergruppe, Frauenklinik der TU Munchen, Munchen, D-81675, Germany

SOURCE: Biological Chemistry (2002), 383(1), 207-216
CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER: Walter de Gruyter GmbH & Co. KG

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 18 Apr 2002

AB The urokinase-type plasminogen activation system, including the serine protease uPA (urokinase-type plasminogen activator) and its cell surface receptor (uPAR, CD87), are important key mols. in tumor invasion and metastasis. Besides its proteolytic function, binding of uPA to uPAR on tumor cells exerts various cell responses such as migration, adhesion, proliferation, and differentiation. Hence, the uPA/uPAR system is a potential target for tumor therapy. We have designed a new generation of uPA-derived synthetic cyclic peptides suited to interfere with the binding of uPA to uPAR and present a new technol. involving micro silica particles coated with uPA (SP-uPA) and reacting with recombinant sol. uPAR (suPAR), to rapidly assess the antagonistic potential of uPA-peptides by flow cytofluorometry (FACS). For this, we used silica particles of 10 .mu.m in diam. to which HMW-uPA is coupled using the EDC/NHS method. Sol., recombinant suPAR was added and the interaction of SP-uPA with suPAR verified by reaction with monoclonal antibody HD13.1 directed to uPAR, followed by a cyan dye (cy5)-labeled antibody directed against mouse IgG. Thereby it was possible to test naturally occurring ligands of uPAR (HMW-uPA, ATF) as well as highly effective, synthetic cyclic uPA-derived peptides (cyclo21,29[D-Cys21Cys29]-uPA21-30, cyclo21,29[D-Cys21Nle28Cys29]-uPA21-30, cyclo21,29[D-Cys212-Nal24Cys29]-uPA21-30, and cyclo21,29[D-Cys21Orn23Thi24Thi25Cys29]-uPA21-30). The results obtained

with the noncellular SP-uPA/uPAR system are highly comparable to those obtained with a cellular system involving FITC-uPA and the promyeloid cell line U937 as the source of uPAR.

IT 321147-43-7P 461681-20-9P 461681-24-3P

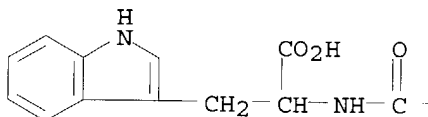
RL: ANT (Analyte); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(a novel anal. system to investigate uPA-uPAR interaction and to test synthetic uPAR antagonists as potential cancer therapeutics)

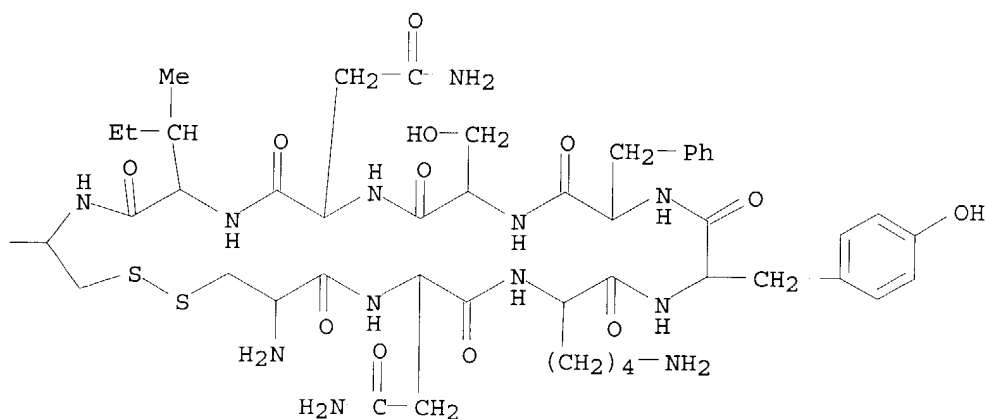
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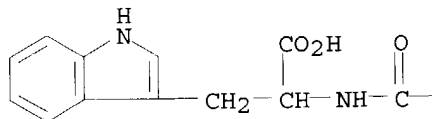
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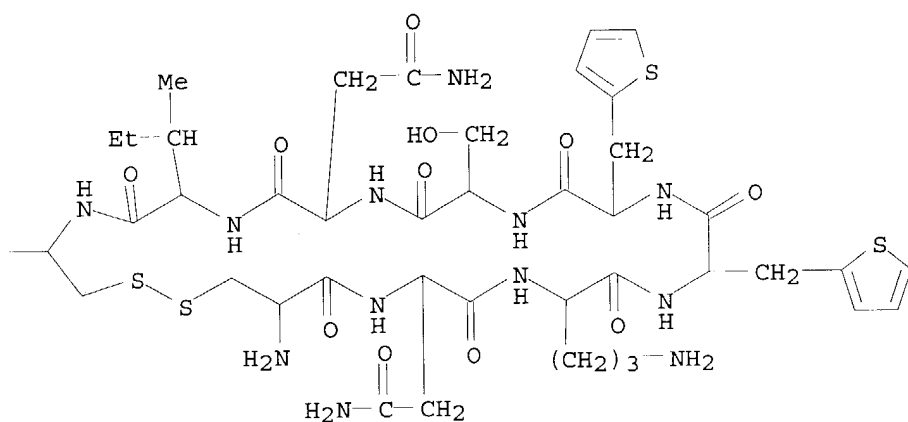
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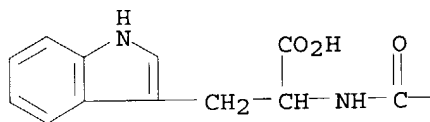


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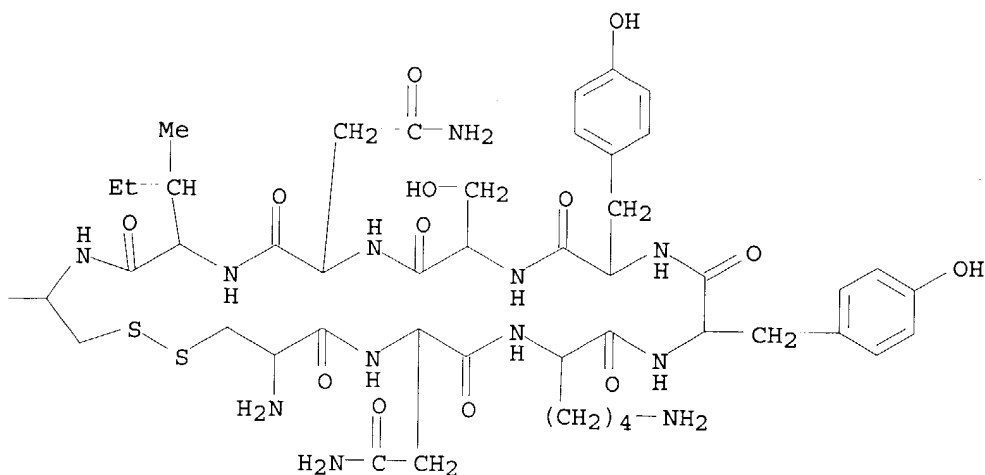


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IT 321147-87-9P

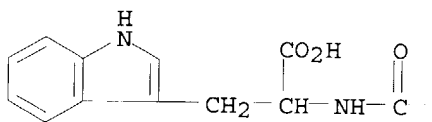
RL: ANT (Analyte); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(h; a novel anal. system to investigate uPA-uPAR interaction and to test synthetic uPAR antagonists as potential cancer therapeutics)

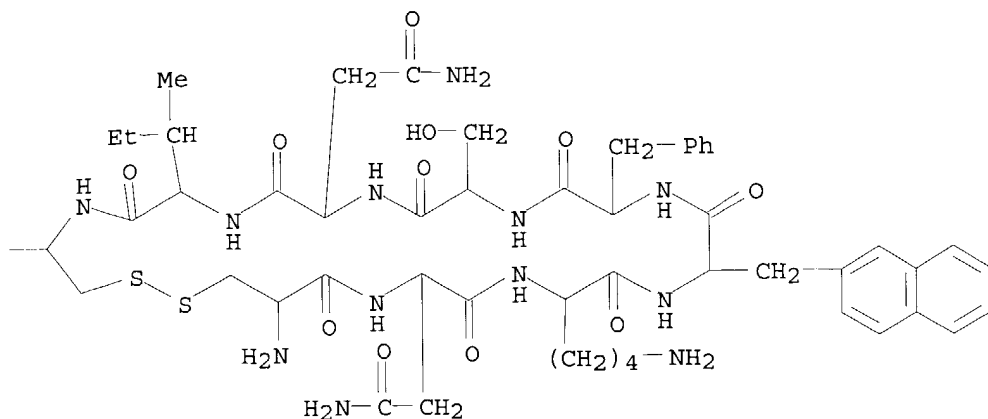
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REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:64013 CAPLUS
DOCUMENT NUMBER: 134:110477
TITLE: Cyclic peptidomimetic urokinase receptor antagonists and therapeutic use thereof
INVENTOR(S): Wilhelm, Olaf; Kessler, Horst; Burple, Markus; Potthoff, Nils; Schmiedeberg, Niko
PATENT ASSIGNEE(S): Willex Biotechnology G.m.b.H., Germany
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2001005811 | A2 | 20010125 | WO 2000-EP6905 | 20000719 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 19933701 | A1 | 20010125 | DE 1999-19933701 | 19990719 |
| EP 1194531 | A2 | 20020410 | EP 2000-951406 | 20000719 |
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| | | | DE 1999-19933701 | A 19990719 |
| | | | WO 2000-EP6905 | W 20000719 |

OTHER SOURCE(S): MARPAT 134:110477

ED Entered STN: 26 Jan 2001

AB Cyclic peptide compds. are provided which are used as inhibitors of urokinase binding to urokinase receptors. The cyclic peptide compds. are

suitable for use as pharmaceutical active ingredients to combat diseases which are mediated by urokinase and urokinase receptor.

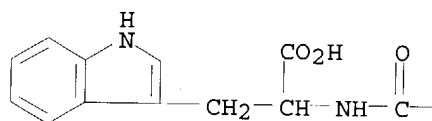
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321147-67-5P 321147-85-7P 321147-91-5P
321147-95-9P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(cyclic peptidomimetic urokinase receptor antagonists and therapeutic use)

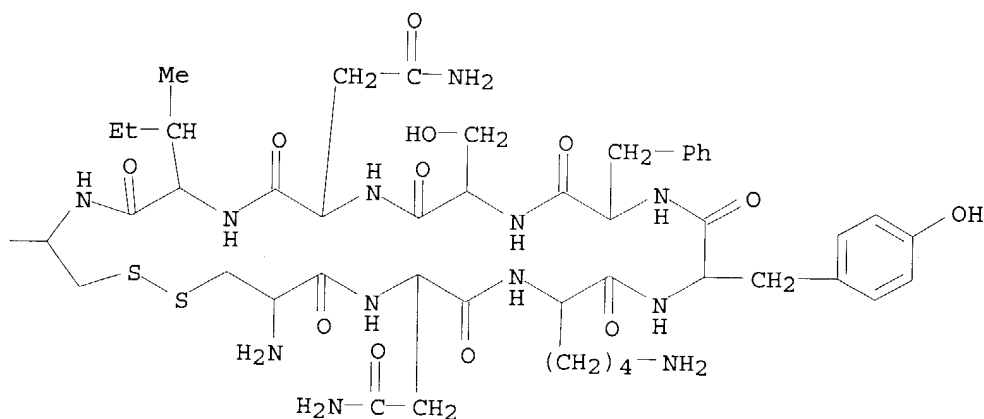
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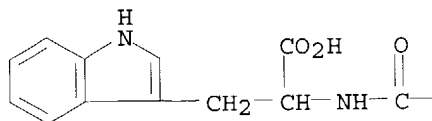
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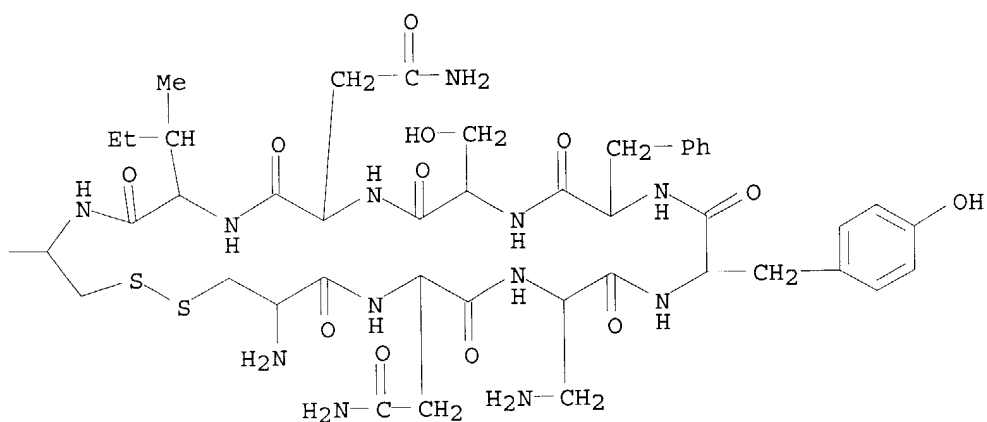
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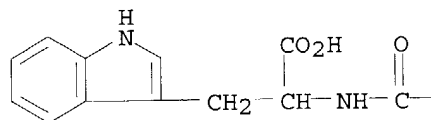


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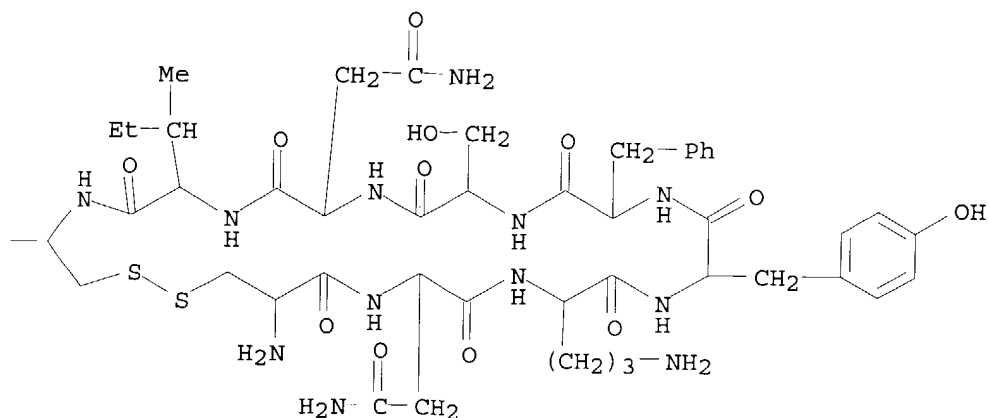


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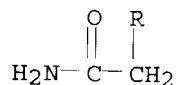
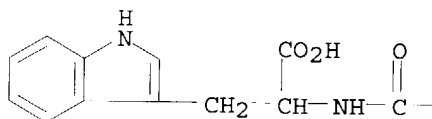


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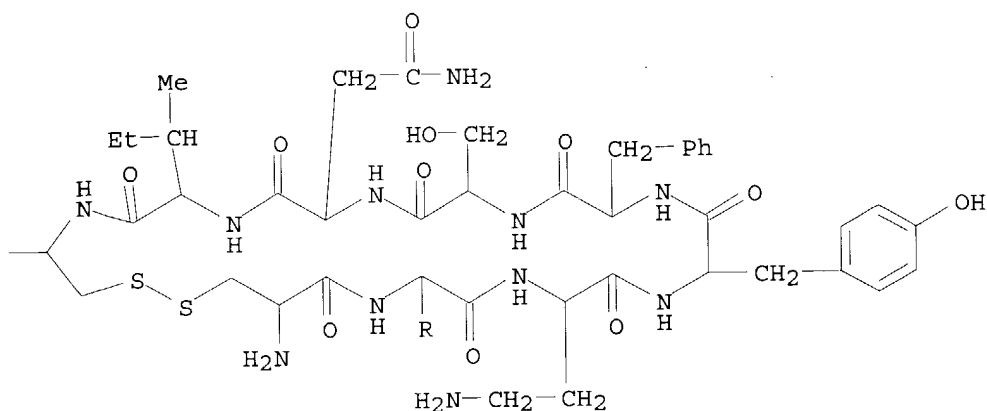


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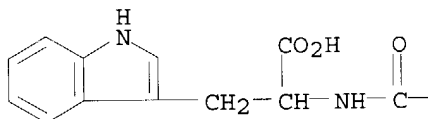


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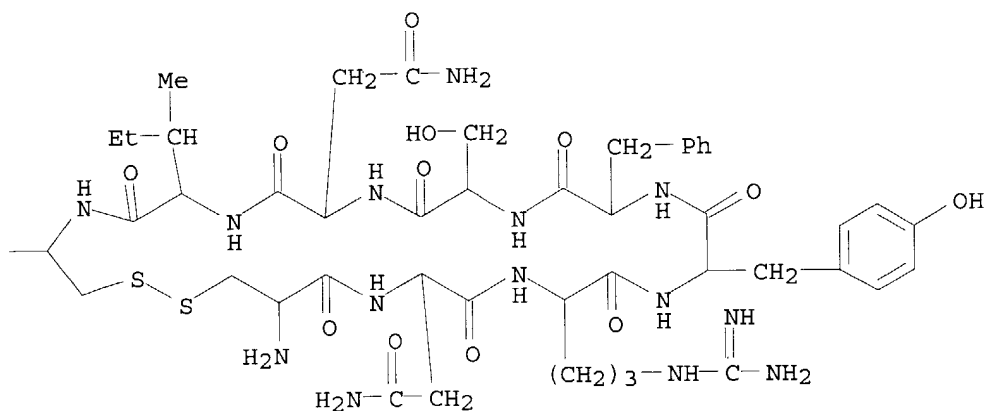


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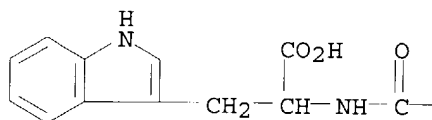
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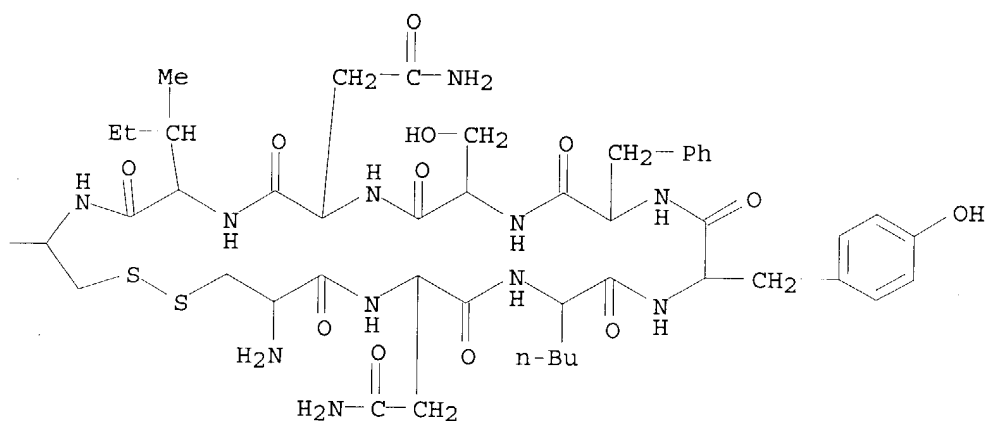
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(1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

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PAGE 1-B

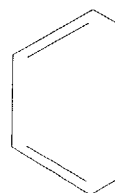


RN 321147-95-9 CAPLUS

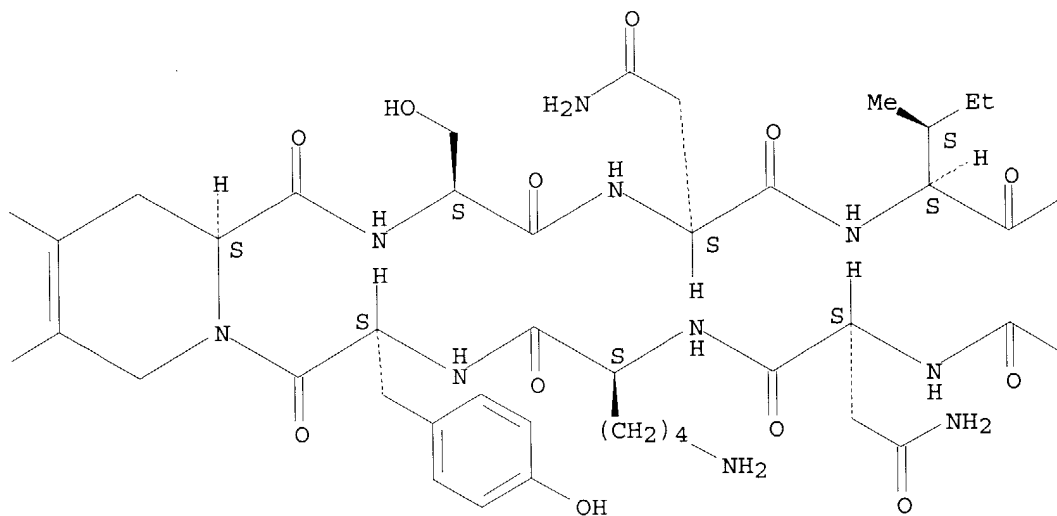
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Absolute stereochemistry.

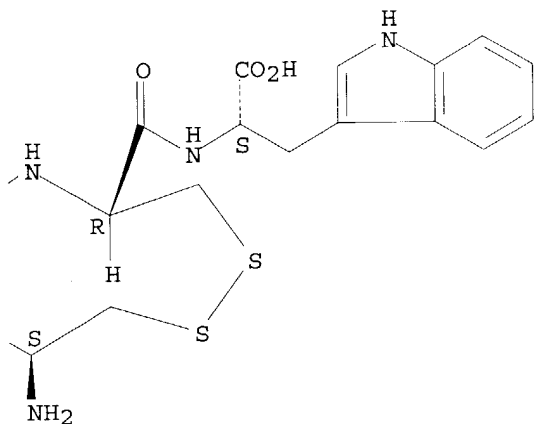
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PAGE 1-C



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 321147-65-3P 321147-69-7P 321147-71-1P
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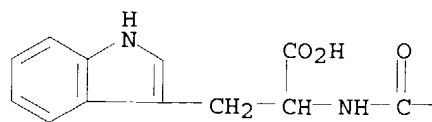
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(cyclic peptidomimetic urokinase receptor antagonists and therapeutic use)

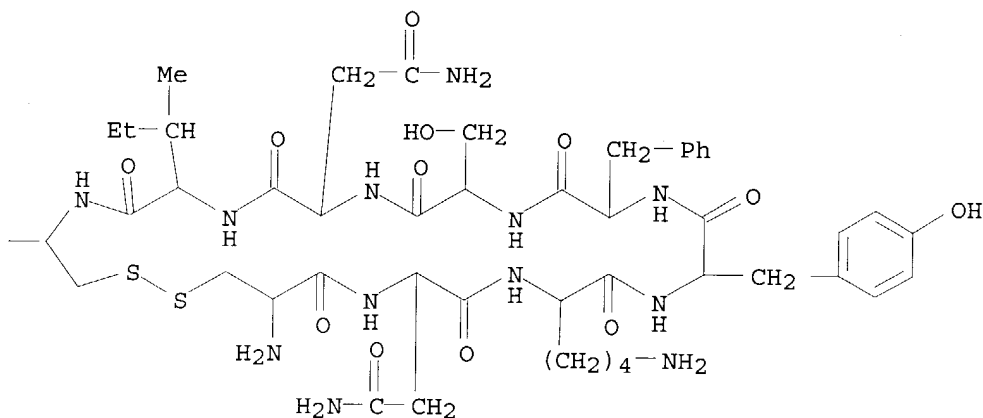
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PAGE 1-A

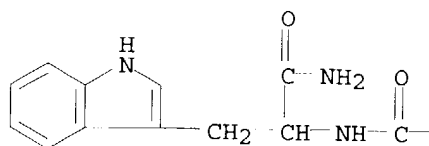


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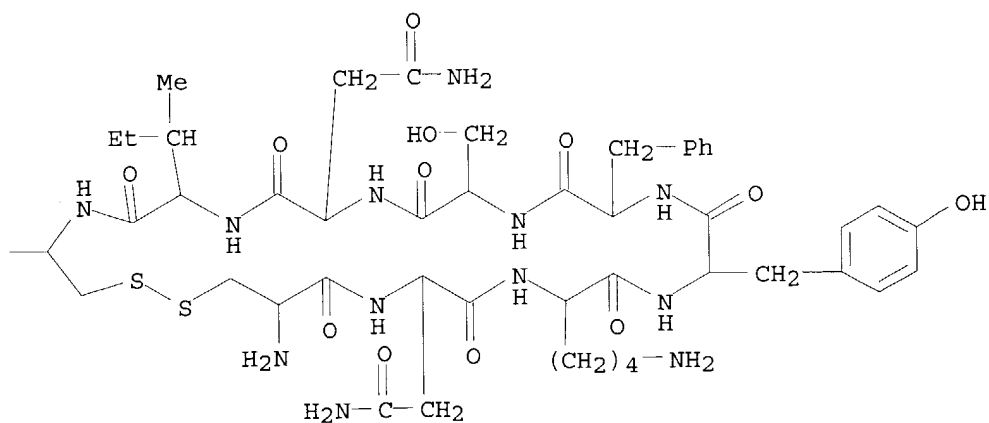


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PAGE 1-A

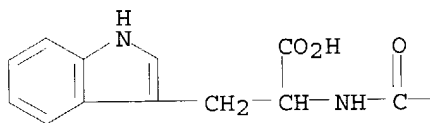


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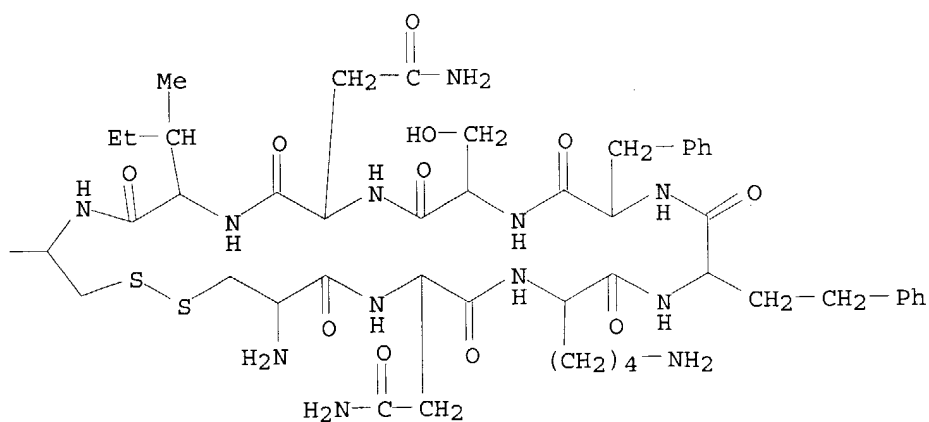


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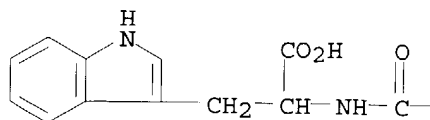
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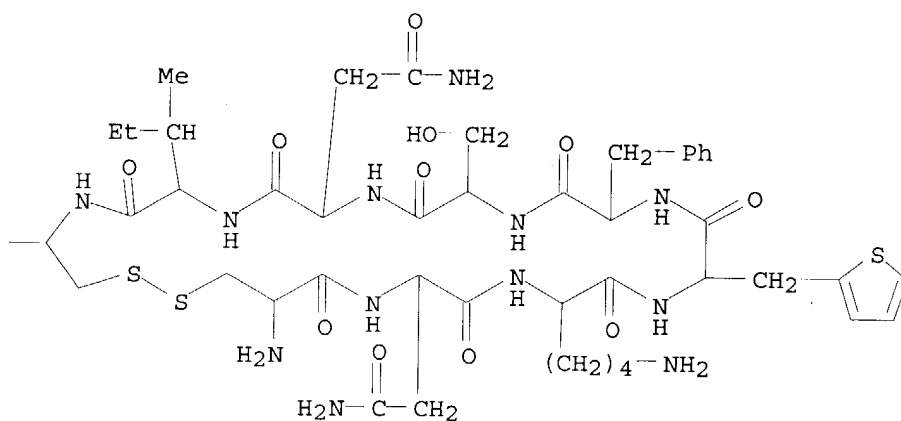
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(1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

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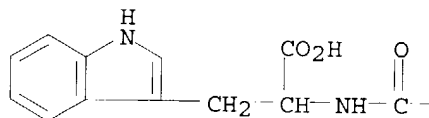


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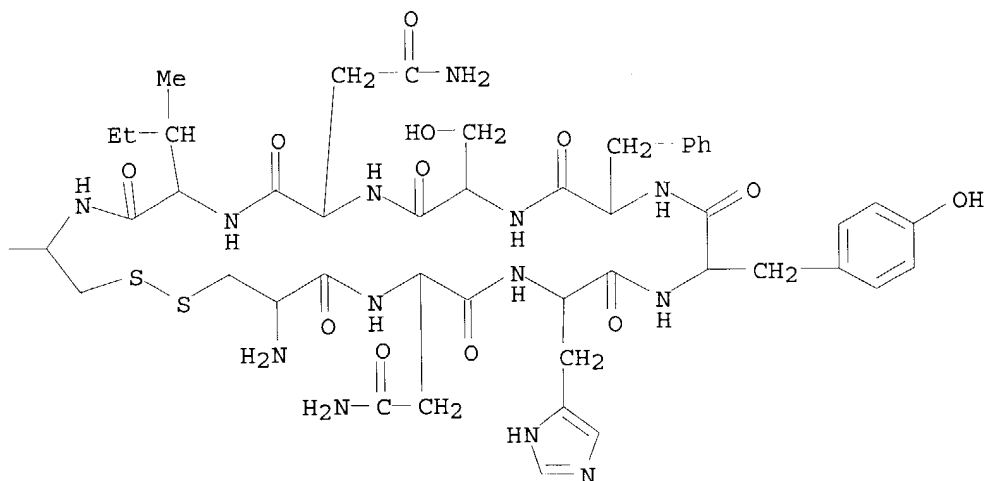


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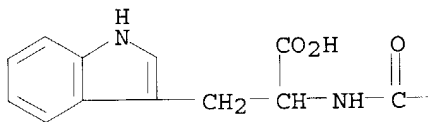


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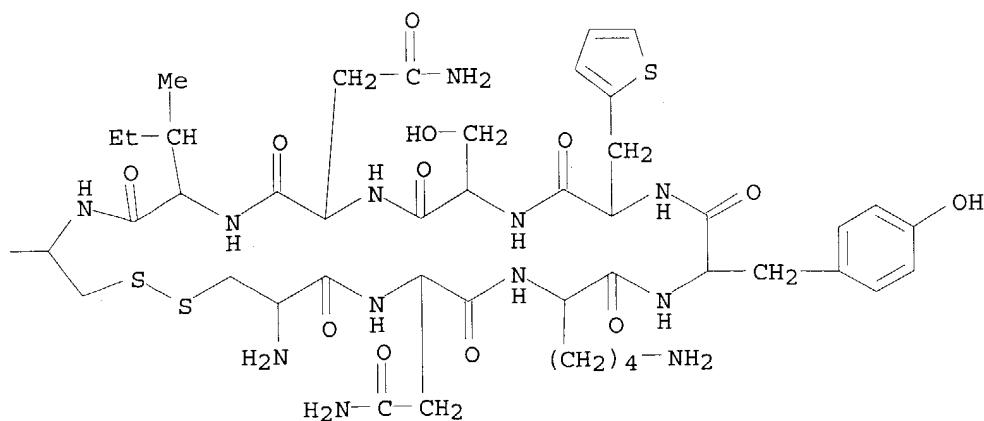


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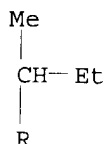
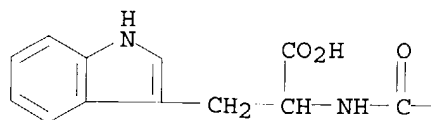


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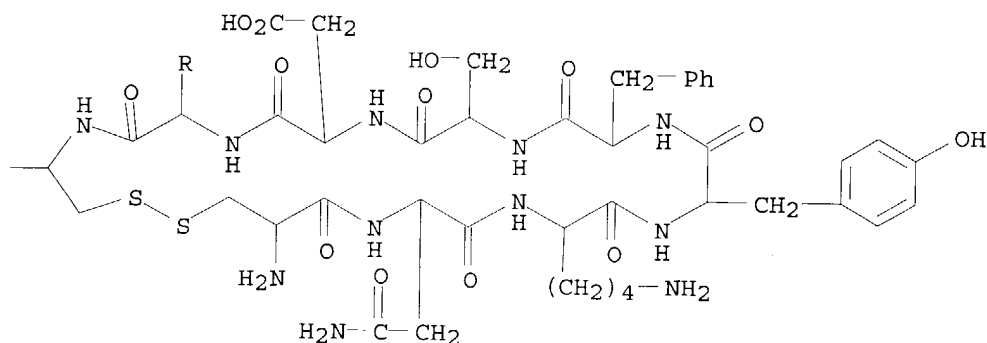


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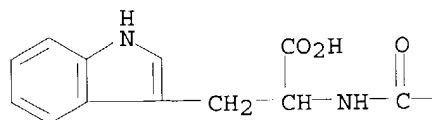


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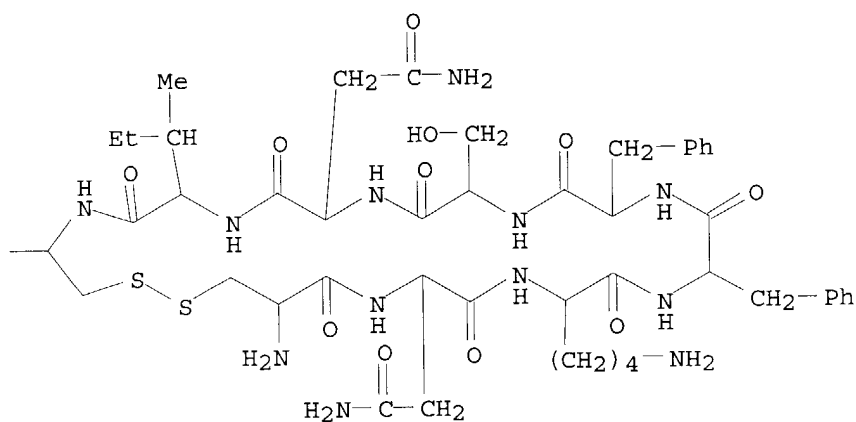


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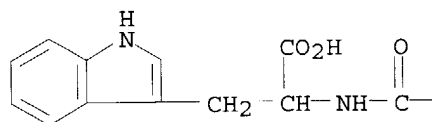


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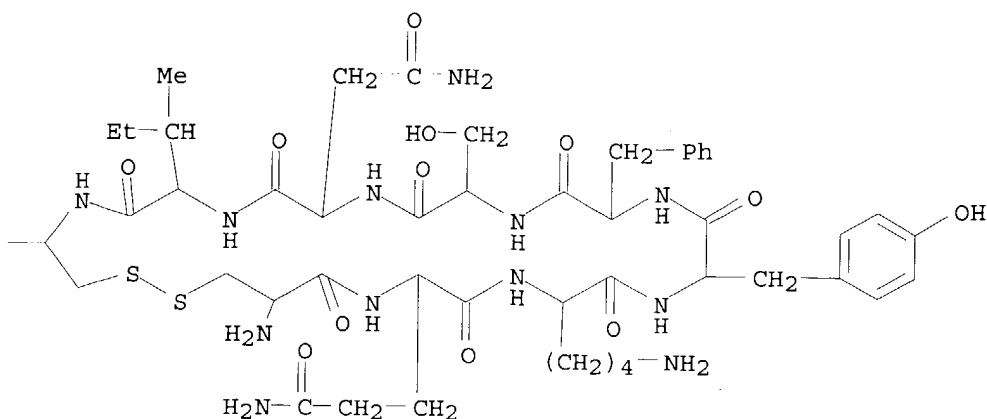


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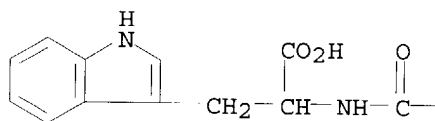


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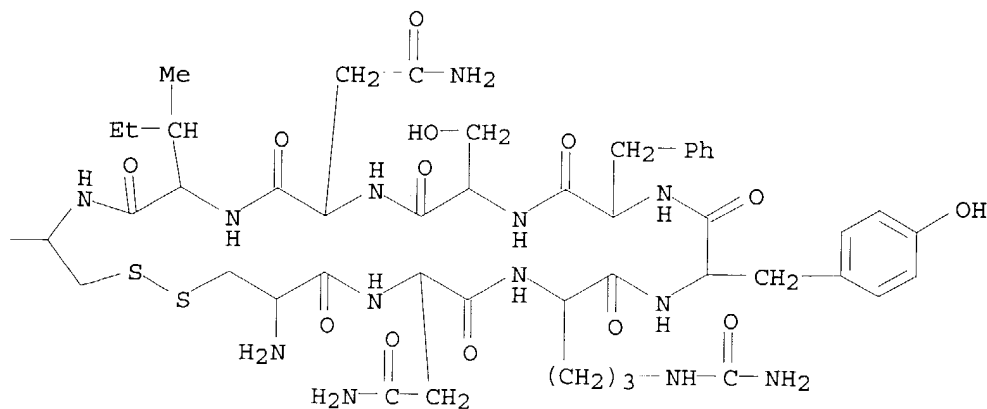


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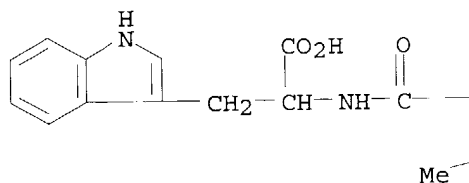
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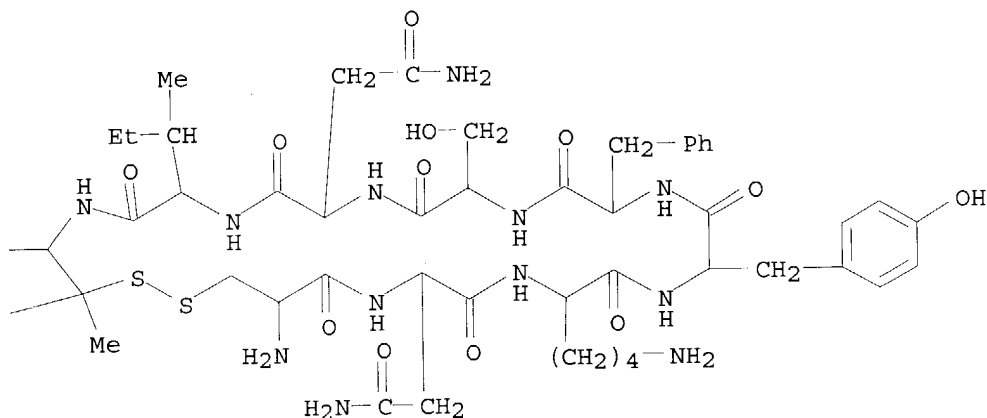
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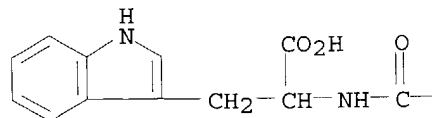


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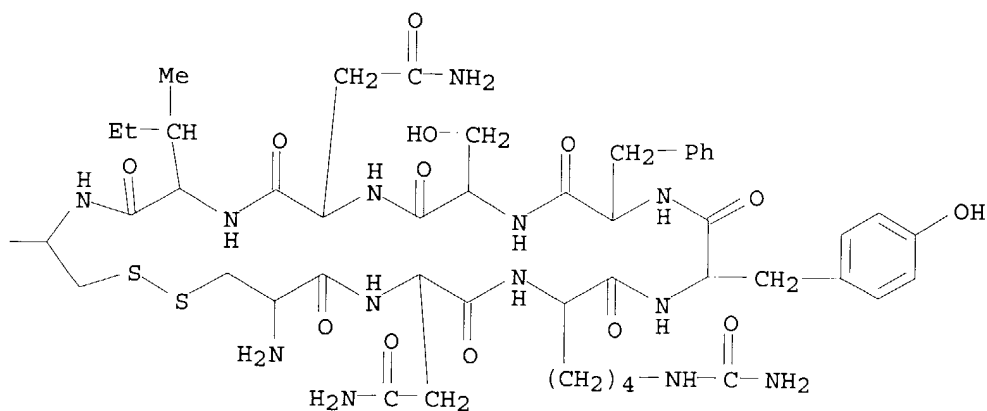


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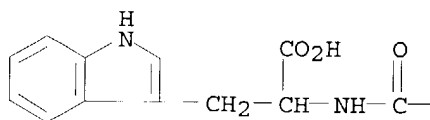


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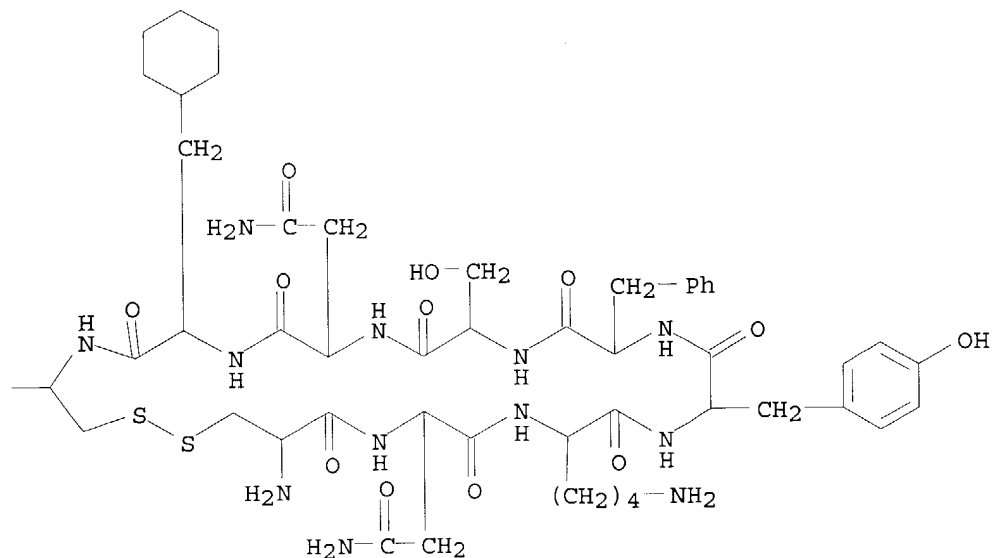


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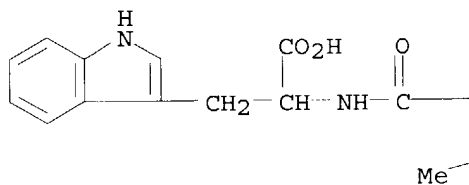


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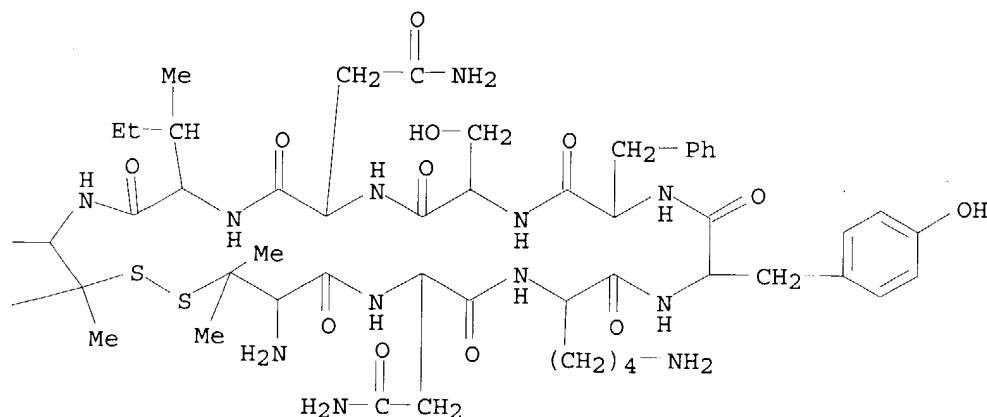


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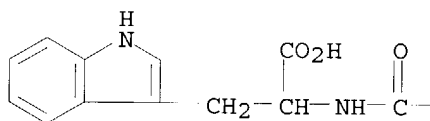
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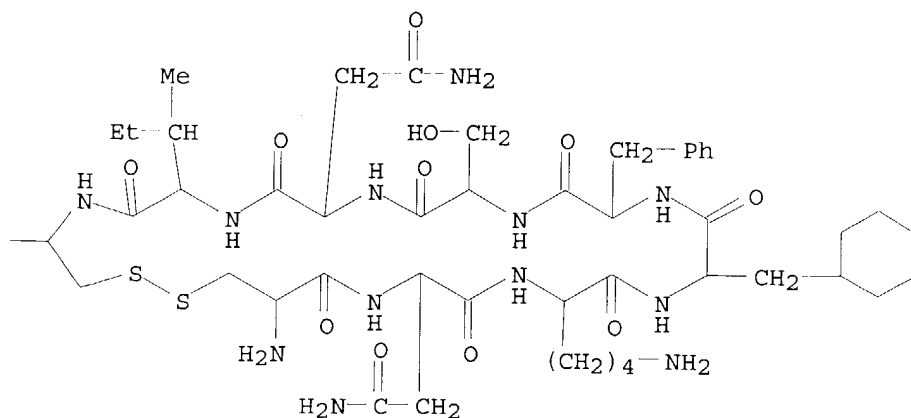
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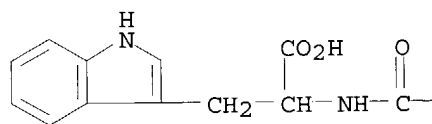


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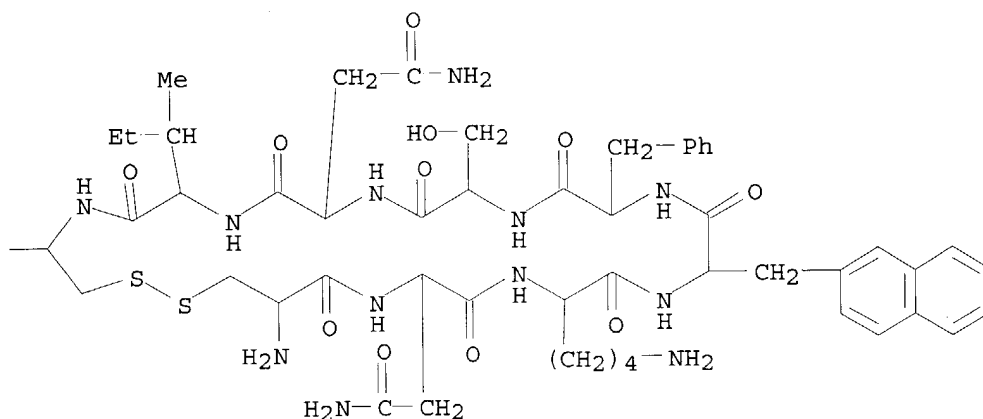
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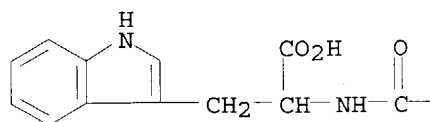


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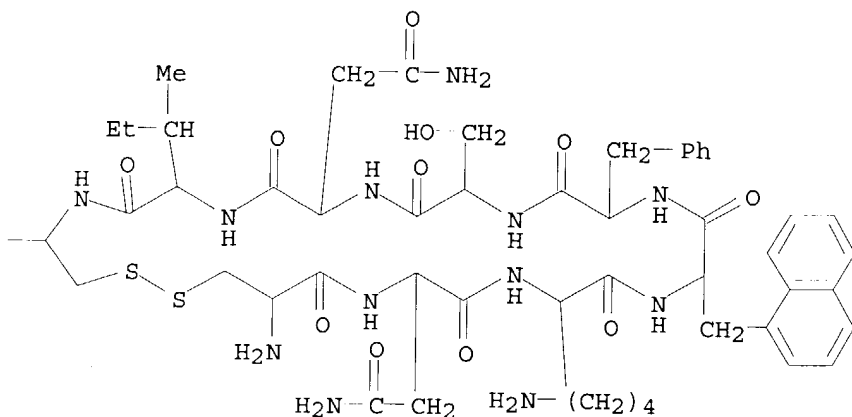


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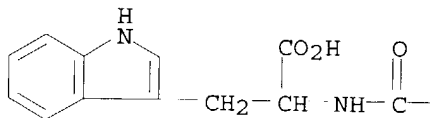


IT 321147-43-7D, amino acid-substitution derivs.
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclic peptidomimetic urokinase receptor antagonists and therapeutic use)

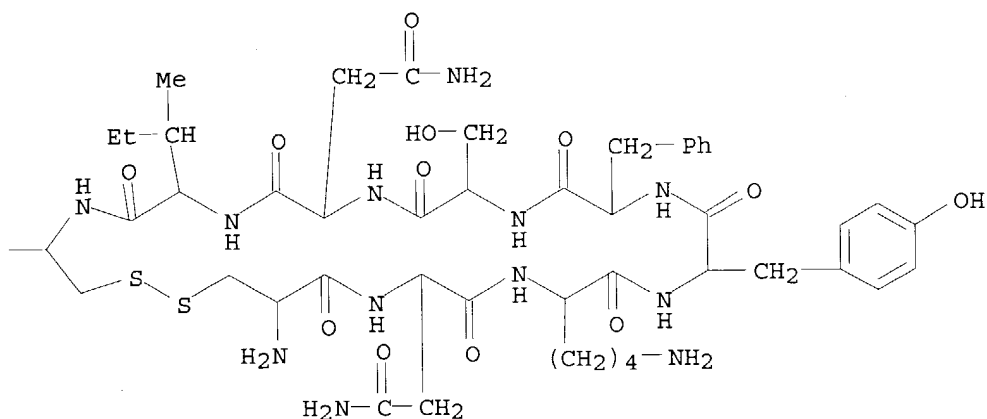
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L6 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
 ACCESSION NUMBER: 1998:716166 CAPLUS
 DOCUMENT NUMBER: 129:310886
 TITLE: Peptide inhibitors of the urokinase receptor
 INVENTOR(S): Kessler, Horst; Graeff, Heinrich; Schmitt, Manfred;
 Magdolen, Viktor; Wilhelm, Olaf G.; Riemer, Christoph;
 Buergle, Markus
 PATENT ASSIGNEE(S): Willex Biotechnology G.m.b.H., Germany
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 9846632 | A2 | 19981022 | WO 1998-EP2179 | 19980414 |
| WO 9846632 | A3 | 19990128 | | |
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| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
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| AU 730333 | B2 | 20010301 | | |
| EP 971948 | A2 | 20000119 | EP 1998-919267 | 19980414 |
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| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2001519823 | T2 | 20011023 | JP 1998-543493 | 19980414 |
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| | | | EP 1997-106024 | A 19970411 |
| | | | WO 1998-EP2179 | W 19980414 |
| | | | US 2000-402464 | A3 20000107 |

OTHER SOURCE(S): MARPAT 129:310886
 ED Entered STN: 11 Nov 1998
 AB Disclosed are peptides as agents for inhibiting urokinase binding to its

receptor. Said peptides, preferably cyclical, are suitable as active agents for treating diseases involving urokinase or the receptor thereof, e.g., tumor metastasis.

IT 214895-18-8P

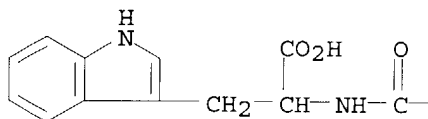
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(peptide inhibitors of the urokinase receptor)

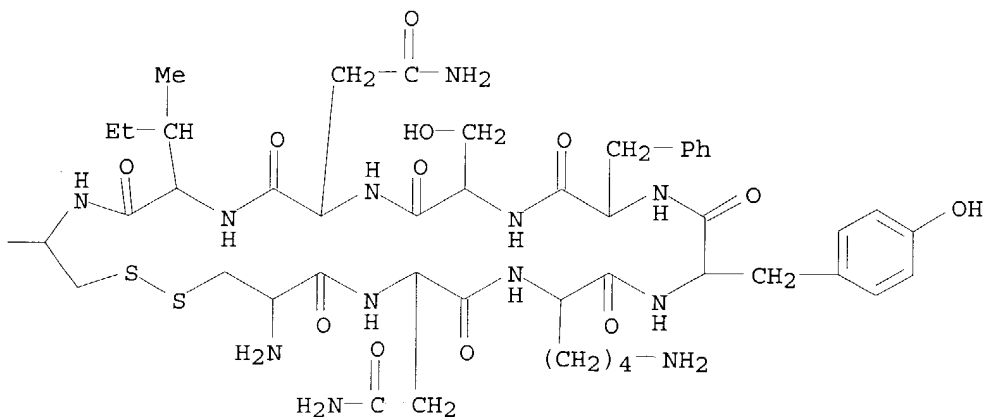
RN 214895-18-8 CAPLUS

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L6 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:240998 CAPLUS

DOCUMENT NUMBER: 138:265592

TITLE: Method for the determination of protein protein interactions by fluorescence measurement

INVENTOR(S): Burgle, Markus; Guthaus, Elke; Schmitt, Manfred; Magdolen, Viktor; Kessler, Horst

PATENT ASSIGNEE(S): Willex AG, Germany

SOURCE: Ger. Offen., 6 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|-------|----------|------------------|-------------|
| ----- | ----- | ----- | ----- | ----- |
| DE 10209030 | A1 | 20030327 | DE 2002-10209030 | 20020301 |
| PRIORITY APPL. INFO. | | | DE 2001-10143768 | IA 20010906 |

PRIORITY APPLN. INFO.:

ED Entered STN: 28 Mar 2003

AB The invention provides a method for the detn. of interactions, in particular protein-protein interactions, by means of fluorescence measurements, as well as suitable reagents and kits. The method is in particular suitable for detg. the influence of test substances on interactions, for example in screening processes for the identification of therapeutic active substances, or for the identification and characterization of new receptor ligands or receptors from biol. samples.

IT 321147-43-7 321147-87-9 461681-20-9

461681-24-3

461681-24-3
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(protein-protein interaction detn. by fluorescence measurement)

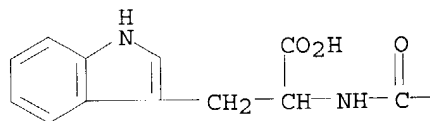
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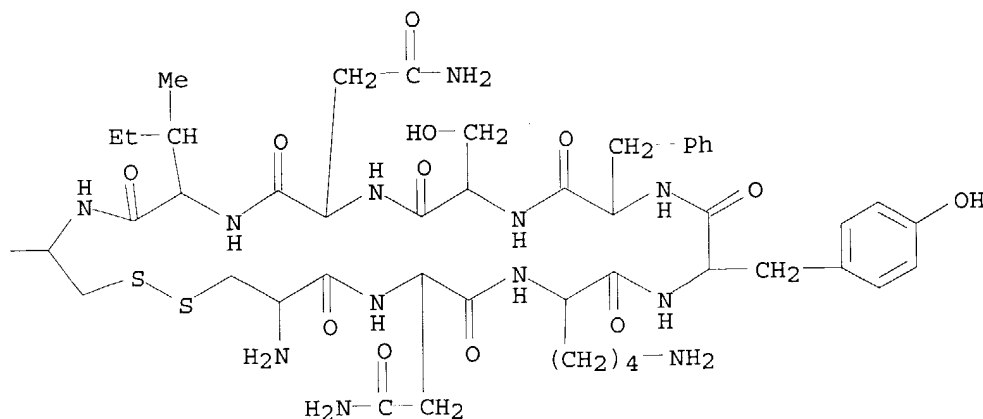
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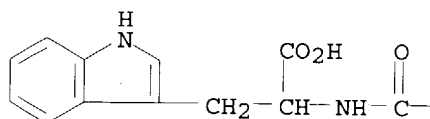


RN 321147-87-9 CAPLUS

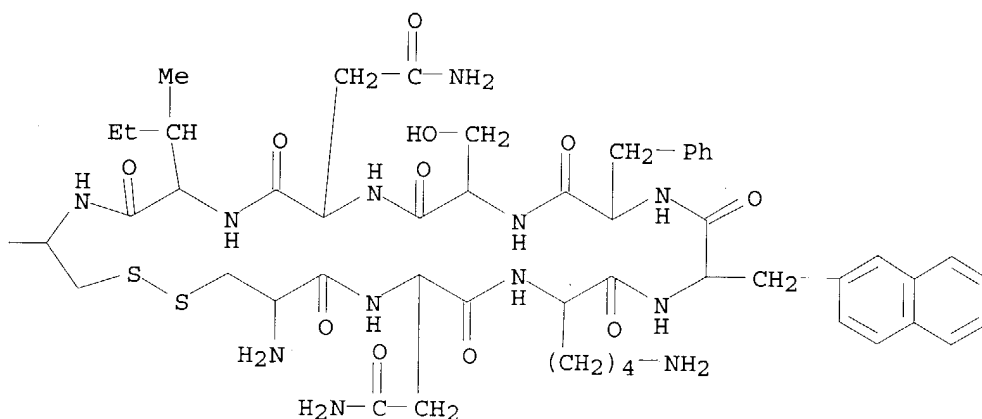
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PAGE 1-A

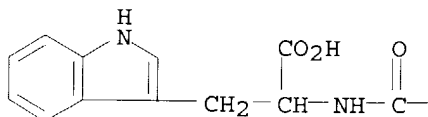


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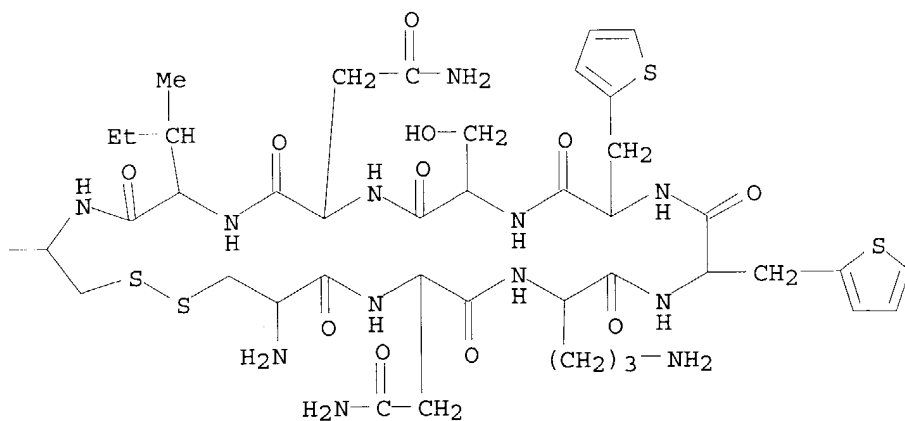


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cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

PAGE 1-A

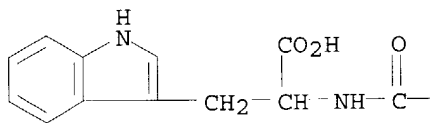


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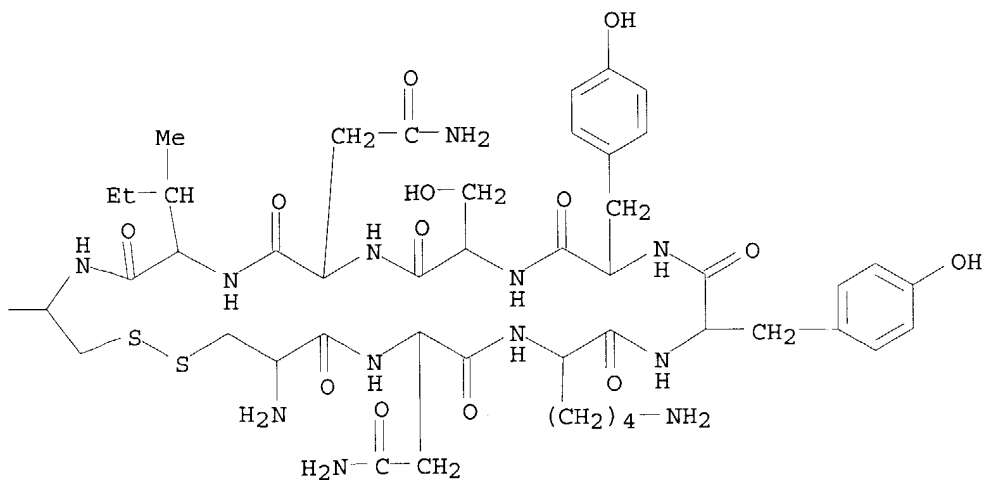


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PAGE 1-B

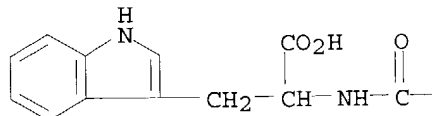


L6 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:158090 CAPLUS
DOCUMENT NUMBER: 136:212777
TITLE: Urokinase antagonist cyclic peptide structure mimetics
and application to drug design
INVENTOR(S): Wilhelm, Olaf; Buergle, Markus; Kessler, Horst;
Schmiedeberg, Niko
PATENT ASSIGNEE(S): Willex A.-G., Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

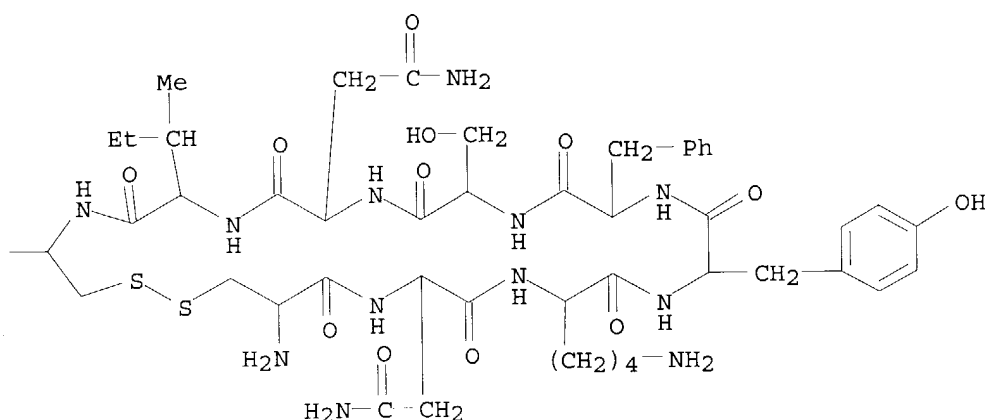
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002016929 | A2 | 20020228 | WO 2001-EP9668 | 20010821 |
| WO 2002016929 | A3 | 20021010 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2002012145 | A5 | 20020304 | AU 2002-12145 | 20010821 |
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| US 2003232389 | A1 | 20031218 | US 2003-362184 | 20030221 |
| PRIORITY APPLN. INFO.: | | | EP 2000-118099 | A 20000823 |
| | | | WO 2001-EP9668 | W 20010821 |

ED Entered STN: 01 Mar 2002
AB The NMR structure of the peptidic urokinase type plasminogen activator antagonist cyclo[21,29][D-Cys21Cys29]-uPA21-30 (cyclo[1,9]D-Cys-Asn-Lys-Tyr-Phe-Ser-Asn-Ile-Cys-Trp) has been solved to identify design strategies for peptidomimetics that interfere with the binding of urokinase type plasminogen activator with its receptor.
IT 321147-43-7
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urokinase antagonist cyclic peptide structure mimetics and application to drug design)
RN 321147-43-7 CAPLUS
CN L-Tryptophan, D-cysteiny-L-asparaginy-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginy-L-isoleucyl-L-cysteiny-L-, cyclic (1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

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L6 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:307896 CAPLUS

DOCUMENT NUMBER: 127:77905

TITLE: Inhibition of the interaction of urokinase-type plasminogen activator (uPA) with its receptor (uPAR) by synthetic peptides

AUTHOR(S): Burgle, Markus; Koppitz, Marcus; Riemer, Christoph; Kessler, Horst; Konig, Bernhard; Weidle, Ulrich H.; Kellermann, Josef; Lottspeich, Friedrich; Graeff, Henner; Schmitt, Manfred; Goretzki, Lothar; Reuning, Ute; Wilhelm, Olaf; Magdolen, Viktor

CORPORATE SOURCE: Institut Organische Chemie Biochemie, Technische Universitat Munchen, Garching, D-85747, Germany

SOURCE: Biological Chemistry (1997), 378(3/4), 231-237
CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER: de Gruyter

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 14 May 1997

AB Focusing of the Ser protease urokinase-type plasminogen activator (uPA) to the cell surface via interaction with its specific receptor (uPAR, CD87) is an important step for tumor cell invasion and metastasis. The ability of a synthetic peptide derived from the uPAR-binding region of uPA (comprising amino acids 16-32 of uPA; uPA16-32) to inhibit binding of fluorescently labeled uPA to uPAR on human promyeloid U937 cells was assessed by quant. flow cytometric anal. (FACS) and compared to the

inhibitory capacities of other synthetic peptides known to interfere with uPA/uPAR-interaction. An about 3000-fold molar excess of uPA16-32 resulted in 50% inhibition of pro-uPA binding to cell surface-associated uPAR. Using a solid-phase uPA-ligand binding assay employing recombinant sol. uPAR coated to microtiter plates, the minimal binding region of wild-type uPA was detd. The linear peptide uPA19-31 and its more stable disulfide-bridged cyclic form (cyclo19,31uPA19-31) displayed uPAR-binding activity whereas other peptides such as uPA18-30, uPA20-32 or uPA20-30 did not react with uPAR. Cyclic peptide derivs. of cyclo19,31uPA19-31 in which certain amino acids were deleted and/or replaced by other amino acids as well as uPAR-derived wild-type peptides did also not inhibit uPA/uPAR-interaction. Cyclo19,31uPA19-31 was identified as a potential lead structure for the development of uPA-peptide analogs to block uPA/uPAR-interaction.

IT 191939-09-0 191939-12-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

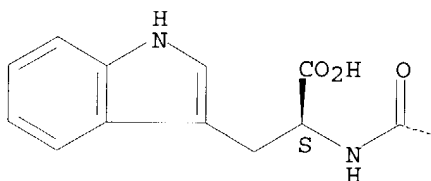
(urokinase-type plasminogen activator interaction with its receptor inhibited by synthetic peptides)

RN 191939-09-0 CAPLUS

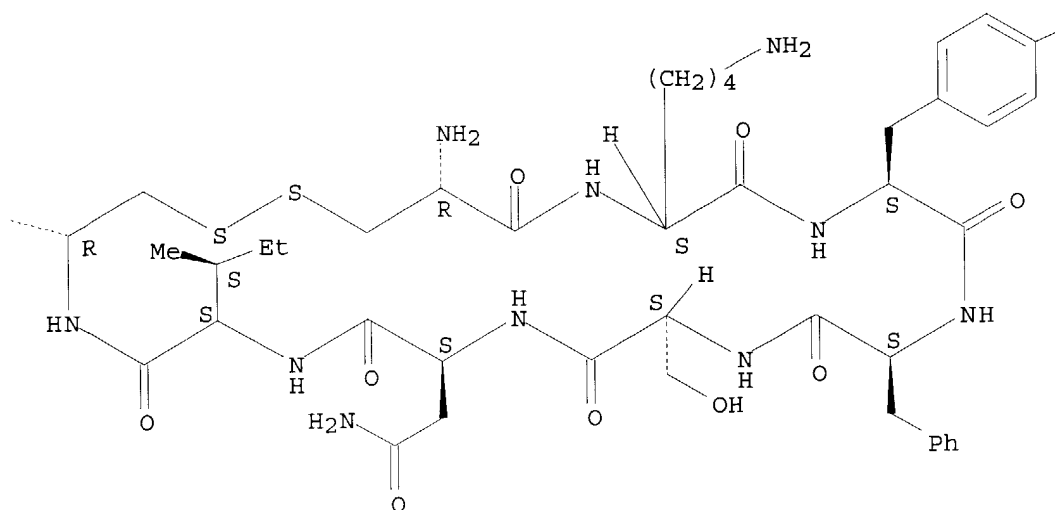
CN L-Tryptophan, L-cysteinyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic (1.fwdarw.8)-disulfide (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B



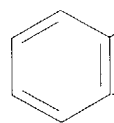
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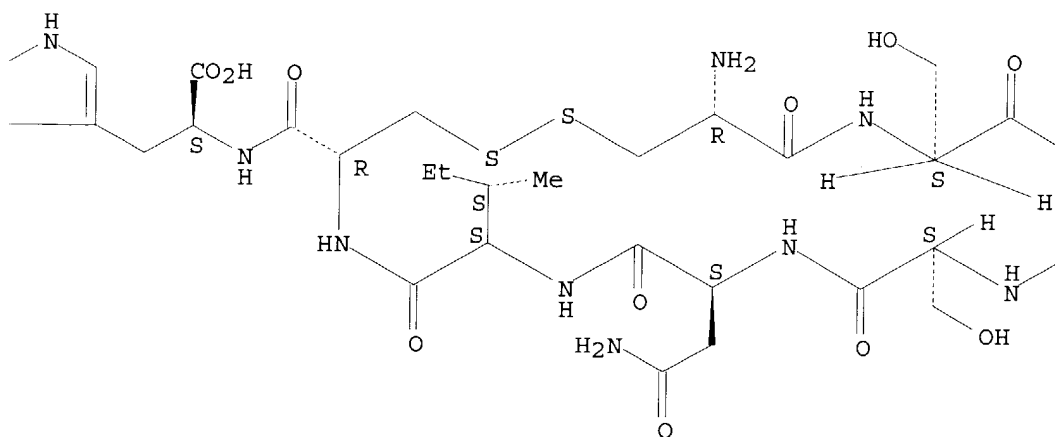
RN 191939-12-5 CAPLUS
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Absolute stereochemistry.

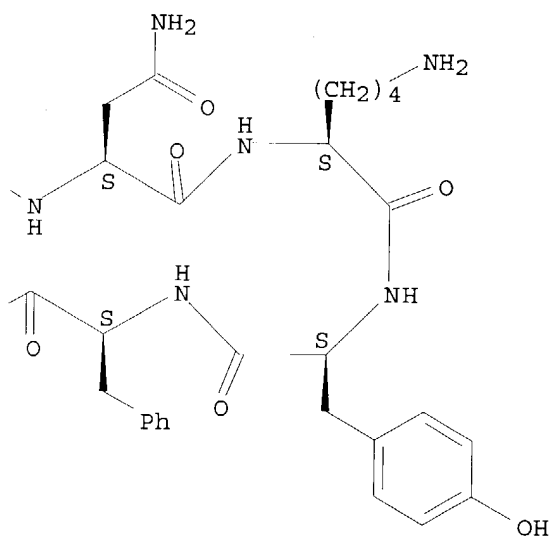
PAGE 1-A



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PAGE 1-C



L6 ANSWER 10 OF 12 USPATFULL on STN
 ACCESSION NUMBER: 2003:330178 USPATFULL
 TITLE: Urokinase peptide structure mimetics
 INVENTOR(S): Wilhelm, Olaf G, UNITED STATES
 Burtle, Markus, M?uuml;nchen, GERMANY, FEDERAL REPUBLIC
 OF
 Kessler, Horst, Schwalbach, GERMANY, FEDERAL REPUBLIC
 OF
 Schmiedeberg, Niko, Rhein, GERMANY, FEDERAL REPUBLIC OF

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2003232389 | A1 | 20031218 |
| APPLICATION INFO.: | US 2003-362184 | A1 | 20030221 (10) |

WO 2001-EP9668

20010821

| | NUMBER | DATE |
|-----------------------|--|----------|
| PRIORITY INFORMATION: | EP 2000-118099 | 20000823 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | ROTHWELL, FIGG, ERNST & MANBECK, P.C., 1425 K STREET, N.W., SUITE 800, WASHINGTON, DC, 20005 | |
| NUMBER OF CLAIMS: | 10 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 8 Drawing Page(s) | |
| LINE COUNT: | 866 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The NMR structure of the peptidic urokinase type plasminogen activator antagonist cyclo[21,29] [D-Cys21Cys29]-uPA.sub.21-30 has been solved to identify design strategies for peptidomimetics that interfere with the binding of urokinase type plasminogen activator with its receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

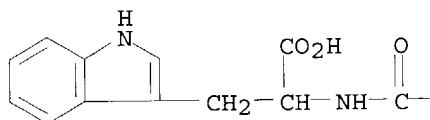
IT 321147-43-7

(urokinase antagonist cyclic peptide structure mimetics and application to drug design)

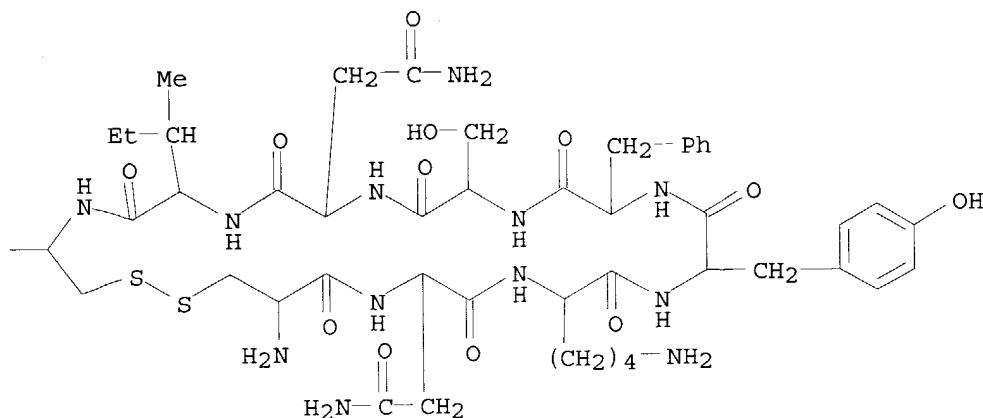
RN 321147-43-7 USPATFULL

CN L-Tryptophan, D-cysteinyl-L-asparaginyl-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginyl-L-isoleucyl-L-cysteinyl-, cyclic
(1.fwdarw.9)-disulfide (9CI) (CA INDEX NAME)

PAGE 1-A

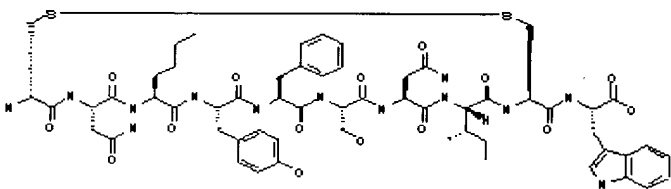


PAGE 1-B



L6 ANSWER 11 OF 12 PROUSDDR COPYRIGHT 2004 PROUS SCIENCE on STN
ACCESSION NUMBER: 2003:906 PROUSDDR
DOCUMENT NUMBER: 328089
CHEMICAL NAME: Cyclo(21-29) (D-Cys21,L-Nle23,L-Cys29)uPA(21-30)
CHEMICAL NAME: D-CysteinyL-L-asparaginyL-L-norleucyL-L-tyrosyL-L-phenylalanyL-L-seryL-L-asparaginyL-L-isoleucyL-L-cysteinyL-L-tryptophan cyclic disulfide
DRUG NAME: WX-360-Nle
CAS REGISTRY NUMBER: 321147-91-5
MOLECULAR FORMULA: C58 H77 N13 O15 S2
HIGHEST DEV. PHASE: PRECLINICAL
ORIGINATOR: Wilex
CLASSIFICATION CODE: Oncolytic Drugs
OTHER SOURCE: PROUSDDR 2003000057 (DDR Preferred)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 9 May 2004

STRUCTURE:



PROUS REFERENCES:

RefID: 706608 (Text Available)
Drug Data Report, Vol. 25, No. 1, pp 84, 2003

REFERENCE TEXT:

RefID: 706608
ACTION - Antineoplastic and antimetastatic agent, a urokinase-derived cyclic peptide shown to inhibit the urokinase plasminogen activator (uPA)/uPA receptor interaction (IC₅₀ = 60 nM). The peptide is resistant to proteolytic cleavage and is stable in blood serum or plasma; it significantly inhibited endothelial cell assembly in rat aortic rings and exhibited low cell toxicity. In mice bearing human ovarian cancer cells, the peptide administered i.p. at a dose of 20 mg/kg for 37 days significantly reduced tumor weight and spread into peritoneum. Another related compound is:

PATENT REFERENCES:

TITLE: Cyclic peptidomimetic urokinase receptor antagonists
INVENTOR(S): Kessler, H.; Wilhelm, O.; Burgle, M.; Potthoff, N.; Schmiedeberg, N.
PATENT ASSIGNEE(S): Wilex
PATENT INFORMATION: DE 19933701 20010125
WO 2001005811 20010125
PRIORITY INFORMATION: DE 1999-33701 19990719

REFERENCES:

(1) RefID: 700044, Periodic Publication

"Synthesis, solution structure, and biological evaluation of urokinase type plasminogen activator (uPA)-derived receptor binding domain mimetics"

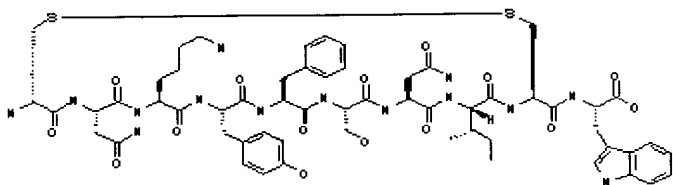
Schmiedeberg, N.; Schmitt, M.; Rolz, C.; et al., J Med Chem, Vol. 45, No. 23, pp 4984, 2002

- (2) RefID: 705858, Periodic Publication
"High-affinity urokinase-derived cyclic peptides inhibiting urokinase/urokinase receptor-interaction: Effects on tumor growth and spread"
Sato, S.; Kopitz, C.; Scmalix, W.A.; Muehlenweg, B.; Kessler, H.; Schmitt, M.; Kruger, A.; Magdolen, V., FEBS Lett, Vol. 528, No. 1-3, pp 212, 2002

L6 ANSWER 12 OF 12 PROUSDDR COPYRIGHT 2004 PROUS SCIENCE on STN

ACCESSION NUMBER: 2003:57 PROUSDDR
DOCUMENT NUMBER: 301479
CHEMICAL NAME: Cyclo(21-29) (D-Cys21,L-Cys29)uPA(21-30)
CHEMICAL NAME: D-Cysteiny-L-asparaginy-L-lysyl-L-tyrosyl-L-phenylalanyl-L-seryl-L-asparaginy-L-isoleucyl-L-cysteiny-L-tryptophan cyclic disulfide
DRUG NAME: WX-360
CAS REGISTRY NUMBER: 321147-43-7
MOLECULAR FORMULA: C58 H78 N14 O15 S2
STATUS: Actively Investigated
HIGHEST DEV. PHASE: PRECLINICAL
ORIGINATOR: Wilex
CLASSIFICATION CODE: Oncolytic Drugs
ACTION MECHANISM: Angiogenesis Inhibitors
OTHER SOURCE: PROUSDDR 2003000906 (DDR Nonpreferred)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 9 May 2004

STRUCTURE:



PROUS REFERENCES:

RefID: 706608 (Text Available)
Drug Data Report, Vol. 25, No. 1, pp 84, 2003

REFERENCE TEXT:

RefID: 706608
ACTION - Antineoplastic and antimetastatic agent, a urokinase-derived cyclic peptide shown to inhibit the urokinase plasminogen activator (uPA)/uPA receptor interaction (IC50 = 60 nM). The peptide is resistant to proteolytic cleavage and is stable in blood serum or plasma; it significantly inhibited endothelial cell assembly in rat aortic rings and exhibited low cell toxicity. In mice bearing human ovarian cancer cells, the peptide administered i.p. at a dose of 20 mg/kg for 37 days significantly reduced tumor weight and spread into peritoneum. Another related compound is:

PATENT REFERENCES:

TITLE: Cyclic peptidomimetic urokinase receptor antagonists
INVENTOR(S): Kessler, H.; Wilhelm, O.; Burgle, M.; Potthoff, N.;
Schmiedeberg, N.
PATENT ASSIGNEE(S): Wilex
PATENT INFORMATION: DE 19933701 20010125
WO 2001005811 20010125
PRIORITY INFORMATION: DE 1999-33701 19990719

TITLE: Urokinase peptide structure mimetics
INVENTOR(S): Kessler, H.; Wilhelm, O.; Burgle, M.; Schmiedeberg, N.
PATENT ASSIGNEE(S): Wilex
PATENT INFORMATION: WO 2002016929 20020228
PRIORITY INFORMATION: EP 2000-118099 20000823

REFERENCES:

- (1) RefID: 620433, Congress Literature
"Inhibitors of the urokinase-type plasminogen activator system as
potent candidates of novel anticancer therapeutics"
Probst, J.C.; et al., Angiogenesis Cancer: Basic Mech Ther Appl, Oct 11
2000-Oct 15 2000, Traverse City, (Abst B21)
- (2) RefID: 611534, Periodic Publication
"Small molecule approach to inhibit the urokinase-type plasminogen
activator system"
Probst, J.C.; Burgle, M.; Foekens, J.; et al., Proc Am Assoc Cancer
Res, Vol. 42, (Abst 370), 2001
- (3) RefID: 663198, Periodic Publication
"Inhibitors of the urokinase-type plasminogen activator system"
Wosikowski, K.; Foekens, J.; Kopitz, C.; et al., Proc Am Assoc Cancer
Res, Vol. 43, (Abst 791), 2002
- (4) RefID: 700044, Periodic Publication
"Synthesis, solution structure, and biological evaluation of urokinase
type plasminogen activator (uPA)-derived receptor binding domain
mimetics"
Schmiedeberg, N.; Schmitt, M.; Rolz, C.; et al., J Med Chem, Vol. 45,
No. 23, pp 4984, 2002
- (5) RefID: 705858, Periodic Publication
"High-affinity urokinase-derived cyclic peptides inhibiting
urokinase/urokinase receptor-interaction: Effects on tumor growth and
spread"
Sato, S.; Kopitz, C.; Scmalix, W.A.; Muehlenweg, B.; Kessler, H.;
Schmitt, M.; Kruger, A.; Magdolen, V., FEBS Lett, Vol. 528, No. 1-3, pp
212, 2002
- (6) RefID: 705859, Periodic Publication
"uPA-silica-Particles (SP-uPA): A novel analytical system to
investigate uPA-uPAR interaction and to test synthetic uPAR antagonists
as potential cancer therapeutics"
Guthaus, E.; Burgle, M.; Schmiedeberg, N.; et al., Biol Chem, Vol. 383,
No. 1, pp 207, 2002

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